International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 09, Issue 04, April 2024,
https://doi.org/10.23958/ijirms/vol09-i04/1855

Original article

Analysis and Presentation of Hospital Antibiogram from a Newly Established Tertiary Care Institute: A Step Towards Antimicrobial Stewardship

Sweta Singh *[1], Sana Islahi [1], Chinmoy Sahu [2], Shefali Gupta [1], Niraj Kumar Srivastava [3], Rajeev Verma [4], Somdatt Sen [5], Vikram Singh Taragi [6]

[1]Assistant Professor, Department of Microbiology, AIIMS, Raebareli, U.P., India.
[2]Additional Professor, Department of Microbiology, SGPGIMS, Lucknow, U.P., India.
[3]Associate Professor, Department of General Surgery, AIIMS, Raebareli, U.P., India.
[4]Assistant Professor, Department of General Medicine, AIIMS, Raebareli, U.P., India.
[5]Research Assistant, Department of Microbiology, AIIMS, Raebareli, U.P., India.
[6]Technical Assistant, Department of Microbiology, AIIMS, Raebareli, U.P., India.

*Corresponding author: Sweta Singh; *swetasinghkarn@gmail.com*

Received 15 March 2024; Accepted 28 March 2024; Published 01 April 2024

Abstract

Introduction: Antimicrobial resistance (AMR) is emerging as a major global threat to public health of the recent times. The local antibiogram provides a guide to the clinicians and helps them choose the best empirical antimicrobial treatment according to the local antibiogram in the event when microbiology culture and susceptibility results are pending. It also helps in monitoring the trends of resistance to the common antimicrobials within the hospital set-up. ***Aims/Objectives:*** This study was planned to determine the prevalence rates of microbial isolates, to appraise and compare the local antibiogram of the newly established institute with established tertiary level centres. ***Materials & Methods:*** This cross sectional study was done for a period of 20 months and samples from outpatient as well as inpatients (from all the wards) were processed in the department of Microbiology. All the samples were processed, routine staining and biochemical tests were employed for preliminary identification of the isolates; followed by antibiotic sensitivity testing. ***Statistical analysis:*** The results were analysed using the SPSS version 22 software (SPSS Inc., Chicago, IL, USA). ***Results:*** The total no. of samples analysed during the specified time period was 20, 987. Overall culture positivity was seen as 36.5%; out of which 56 % was attributed to Gram negative bacteria and the rest by gram positive bacteria and fungal isolates. E.coli showed a sensitivity of 63% / 78% / 58% (AIIMS RBL/ICMR/Tertiary institute) to Amikacin, Meropenem: 53/69/54 %, Imipenem: 62 / 64/ 61 %, Colistin: 98 /99/ 97 %. Klebsiella showed a sensitivity of 38/46/30 % (AIIMS RBL/ICMR/Tertiary institute) to Amikacin, Meropenem: 32/40/26 %, Imipenem: 39/43/30 %, Colistin: 93/96/92%. In the second line antibiotic sensitivity; Fosfomycin in E.coli showed 98%sensitivity, whereas for Klebsiella it was 94% and for pseudomonas 91%.56 % cases of MRSA were isolated in 2021-22 as compared to 54 % in 2022-23. ***Discussion:*** The analysed antibiogram suggests that urinary tract (UTIs), respiratory and pyogenic infections were the most common reasons for ordering culture and sensitivity tests in our setting. A lower percentage of sensitivity to amikacin, carbapenems and colistin as compared to the ICMR data was seen among the Gram-negative isolates of the present study. This might be related to the easy availability as over the counter medications and irrational use of these drugs in this study area. The predominant isolates in our study i.e.*E. coli* and *Klebsiella* spp. were resistant to the cephalosporins, aminoglycosides, etc.This reflected that the Multidrug resistant organisms isolated from various body site infections with resistance to third-generation cephalosporin and other routinely prescribed antibiotics is a major concern in this particular area of interest. ***Conclusion:*** This study provides an elaborately made antibiogram profile of approximately two years from the diagnostic microbiology laboratory of a newly established tertiary level institute catering to the needs of thousands of local population. Antibiotic policy along with local antibiogram is the stepping stone towards accreditation of any hospital setting as well as implementation of antimicrobial stewardship program.

Keywords: ***Antimicrobial resistance- antibiogram- empirical- antimicrobial- Antibiotic policy.***

Introduction

Antimicrobial resistance (AMR) is emerging as a major menace and a serious threat to local population in the coming times. Infections caused by multi-drug resistant (MDR) pathogens fail to respond to initial or first line drugs, which results in longer hospital stay and increased mortality rates. Loss of sensitivity to first line group of antibiotics leads to longer periods of infection with multi-drug resistant organisms and increased numbers of infected people moving in the local population [1]. This in turn poses a high risk of transmission of MDR pathogens as well as resistance genes to the general population.

With the advent of newer diagnostic modalities as well as treatment regimens the life expectancy has increased leading to a rise

in the elderly population. Extremes of age are much more vulnerable to Nosocomial infections and HAIs; further increasing the morbidity and mortality rates due to MDR organisms. Longer hospital stay incurs financial instability and liability not only on individual families but also as a whole on the community.

Approximately 25% of the 60 million year-based deaths worldwide is due to infections caused by Multidrug resistant organisms. There has been significant leap and advances in various diagnostic modalities, infection control practices, antimicrobial stewardship programmes but still; infections with multidrug resistant organisms remains a significant cause of morbidity and mortality among both the in and out patients of developed as well as developing countries [2]. In 2015, WHO launched the "Global Antimicrobial Resistance and Use Surveillance System (GLASS)" with the aim to monitor the increasing AMR rates and also to implement the strategies to contain these increasing trends of resistance. GLASS system monitors the trends of increasing resistance in commonly isolated organisms as well as invasive fungal species and also caters to the One Health surveillance model of human health.

The fourth GLASS report summarizes the 2019 data from 15 countries and 3, 106, 602 lab confirmed isolates and it was reported to WHO in 2020. While, the first call in 2017 reported AMR data of 507, 923 lab confirmed isolates [3]. The rising resistance in nosocomial infections is mainly attributable to the ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumanii, Pseudomonas aeruginosa, and Enterobacter species*).

Easy availability of over the counter drugs and institution of antibiotics in the patients without proper sensitivity testing leads to emergence of early resistance in the old and currently used antimicrobials [3].

Antimicrobial stewardship program (AMSP) forms the cornerstone and provides measures to contain the rates of increasing AMR by rationalizing the use of antimicrobials in the hospital. CDC has defined "Antimicrobial stewardship" as-The **right** antibiotic, for the **right** patient, at the **right** time, with the **right** dose, and the **right** route, causing the least harm to the patient and future patients. World Health Organization (WHO) has emphasized the key role of the microbiology laboratory and a microbiologist in antimicrobial stewardship (AMS) by guiding the clinicians on the appropriate and rational use of antibiotics through formulation of antibiograms [4]. Comprehensive data on the antibiotic sensitivity patterns of bacterial pathogens isolated from different samples and wards is needed for compiling an antibiogram for a particular health set-up. The local antibiogram provides a guide to the clinicians and helps them choose the best empirical antimicrobial treatment according to the local antibiogram in the event when microbiology culture and susceptibility results are pending. It also helps in monitoring the trends of resistance to the common antimicrobials within the hospital set -up as well as to Compare the susceptibility rates across institutions and track resistance trends. Hence, the local antibiogram from a hospital setting may contribute to the national AMR surveillance database as well [5].

Antibiogram data must always be formulated from an accredited or a certified diagnostic microbiology laboratories which uses standard guidelines like the Clinical Laboratory Standards Institute (CLSI) M39-A4 consensus document [6] to ensure accuracy as well as reliability. As AMR is on a rise, antibiogram serves as a useful weapon to fight this impending doom by providing evidence-base data for prescribing empirical treatment as per the WHO essential Medicines List using the Access, Aware, and Reserve (AWaRe) classification [7-9]. Antimicrobial stewardship program relies solely on the Surveillance data of rising AMR trends and this can prove to be an effective tool in evidence-based decision making [8,9].

Therefore, this study was planned to determine the prevalence rates of microbial isolates, to appraise and compare the local antibiogram of the newly established institute with established tertiary level centres.

Methods

Study Setting: The study was done for a period of 20 months from August 2021 to April 2023 and samples from outpatient as well as inpatients (from all the wards) were processed in the department of Microbiology at AIIMS, Raebareli.

Study design: cross sectional study

Sample size: Convenient sampling was done and all the samples during the specified time period were used for analysis in the study.

Ethical clearance: Institutional ethics committee (IEC) permission was taken before the study (IEC Code: 2023-6-IMP-EXP-5). This was a retrospective study from the patients records, hence obtaining informed consent from all participants was not applicable. However, all the protocols and methods used in the study were performed in accordance with relevant guidelines and regulations.

Inclusion criteria: Patients of all age groups from both the OPD and IPD /wards were included in the study. Only the first isolate recovered during the specified time period per patient with confirmed identification and susceptibility testing results was included for analysis. This isolate would be used for analysis regardless of the type of specimen, site, sensitivity profile, etc [10].

Exclusion Criteria: The following were excluded from the study:

- Isolates of screening or surveillance cultures,
- Isolates with ambiguous or intermediate sensitivity results.,
- Duplicate isolate from the same patient.

Sample processing:

A. **Culture:** Specimens to be included in the analysis for the study were: Urine, body fluids (peritoneal fluid, synovial fluid, ascitic fluid and pleural fluid), pus, respiratory specimens like sputum, tracheal aspirate, bronchoalveolar lavage (BAL); cerebrospinal fluid (CSF); blood; swabs from surgical site infections or wounds. All the samples were processed according to standard operating procedures of the laboratory [11]. Blood cultures were done by automated methods using Bact/ALERT 3D system (BioMerieux Inc., Durham, USA) and final results were dispatched after 5 days of incubation [12]. Blood culture bottles which flagged positive in the machine as well as other samples were initially grown on routine medias like blood agar and MacConkey agar for 18-24 hours at 37 °C. Chocolate agar was also used for sterile body fluids and CSF samples. After initial cultures, colonies were identified and subculturing was done as appropriate.

B. **Identification: Routine biochemical testing:** Routine staining and biochemical tests were employed for preliminary identification of the isolates in our laboratory.

C. **Antibiotic sensitivity testing:** Kirby- Bauer's disk diffusion method on Muller Hinton agar were used for antibiotic sensitivity testing and interpreted based on Clinical and Laboratory Standards Institute (CLSI) and EUCAST guidelines [13,14]. MICs were further recorded as per CLSI guidelines for the following drugs: Vancomycin, Linezolid for Gram positive cocci and Colistin, Tigecycline for Gram negative bacilli respectively.

Data collection: As this was a retrospective study, hence the data was retrieved through the Hospital Management information system (HMIS).

Outcome measures: The study analysed the data from 2019 and 2020 based on the frequency of isolated bacteria, their antibiotic sensitivity patterns and the trends of changing AMR patterns in the institute.

D. **Realistic comparison:** Comparison of the antibiogram data was done with an established tertiary level centre and ICMR recent census for resistance patterns of different drugs and organisms.

Statistical Analysis

The results were analysed using the SPSS version 22 software (SPSS Inc., Chicago, IL, USA). Frequencies and percentages were calculated for bacterial isolates and antibiotic sensitivity rates for 2019 and 2020, and comparison was done using the chi-square. Fisher's exact test was also used. Statistical significance was set at $p < 0.05$, and highly statistically significant was at $p \leq 0.001$. The frequencies were shown with 95% confidence intervals (95%CI). The Chi-square and Mann-Whitney U test was used to analyse the statistically significant variables.

Results

Distribution of samples and frequency of Isolates

The total no.of samples analysed during the specified time period was 20, 987.Out of which;67.5% was contributed by urine and 15.2%, 8%, 6%, 3% respectively by respiratory samples, Pus, Blood and body fluids. Culture positivity was seen as 20% for urine, 65% for pus, 54 % for body fluids, 53% for sputum, 21 % for blood and 6% for CSF samples.; accounting for an overall culture positivity of 36.5%.

Among the culture positive cases, 56 % was attributed to Gram negative bacteria and the rest by gram positive bacteria and fungal isolates. Overall; Escherichia coli, Klebsiella and Staphylococcus species were implicated in majority of culture positive samples. On further categorization of the isolates sample wise; E, coli (42%), Klebsiella (19%) and Enterococcus faecalis (15%) were the most common isolates in urine specimen. E, coli (29 %), Pseudomonas aeruginosa (27 %), Klebsiella (19 %) and Acinetobacter baumanii (11%) were seen in majority in respiratory samples. Pus and body fluids saw the predominance of E, coli (29 %), Pseudomonas aeruginosa (19 %), Klebsiella (15 %) and coagulase negative staphylococcus species (14%). Among the blood samples, E.coli (24%) and coagulase negative staphylococcus species (23%) were in majority followed by Klebsiella (14%), Acinetobacter (9%), staphylococcus aureus(14%) and Candida species (5%).Coagulase negative Staphylococcus species (CONS) was present in 53% of the blood isolates as compared to 43 % of Staphylococcus aureus.

Antimicrobial susceptibility testing results

To obtain a realistic picture, we compared our data with the standard ICMR data and with an established tertiary level centre data for regional/local comparison. E.coli showed a sensitivity of 63% / 78% /58% (AIIMS RBL/ICMR/Tertiary institute) to Amikacin, Meropenem: 53/69/54 %, Imipenem: 62 / 64/ 61 %, Colistin: 98 /99/ 97 %. **(Fig 1)** Klebsiella showed a sensitivity of 38/46/30 % (AIIMS RBL/ICMR/Tertiary institute) to Amikacin, Meropenem: 32/40/26 %, Imipenem: 39/43/30 %, Colistin: 93/96/92%. **(Fig 2)** For Staphylococcus aureus, the sensitivity for fluoroquinolones was 32/17/29%; Vancomycin: 100/100/100%, Clindamycin: 58/74/47 %, Teicoplanin:98/98/100% **(Fig 3).**

In the second line antibiotic sensitivity; Fosfomycin in E.coli showed 98%sensitivity, whereas for Klebsiella it was 94% and for pseudomonas 91%.Whereas;Colistin showed a sensitivity rates of 98% for E.coli, 97% for Klebsiella and 96% for pseudomonas **(Fig 4 & 5)**. Minocycline showed sensitivity rates of 88%, 72%, 63% for E.coli, Klebsiella and pseudomonas respectively whereas; Tigecycline showed 88%, 81%, 94% sensitivity rates for E.coli, Klebsiella and Acinetobacter respectively. **(Fig 6 & 7)**

Comparison between year wise trends in MDR isolates (2021-22 vs 2022-23)

56 % cases of MRSA were isolated in 2021-22 as compared to 54 % in 2022-23. Speaking of the rates of isolation of carbapenem resistant Acinetobacter species; 77% and 81% was seen in 2021-22 and 2022-23 respectively. Colistin resistant Klebsiella species were seen as 7% vs 9%, Carbapenem resistant *Pseudomonas aeruginosa* as 40% vs 47% and VRE (Vancomycin resistant Enterococci) as 13% vs 15% in 2021-22 vs 2022-23.

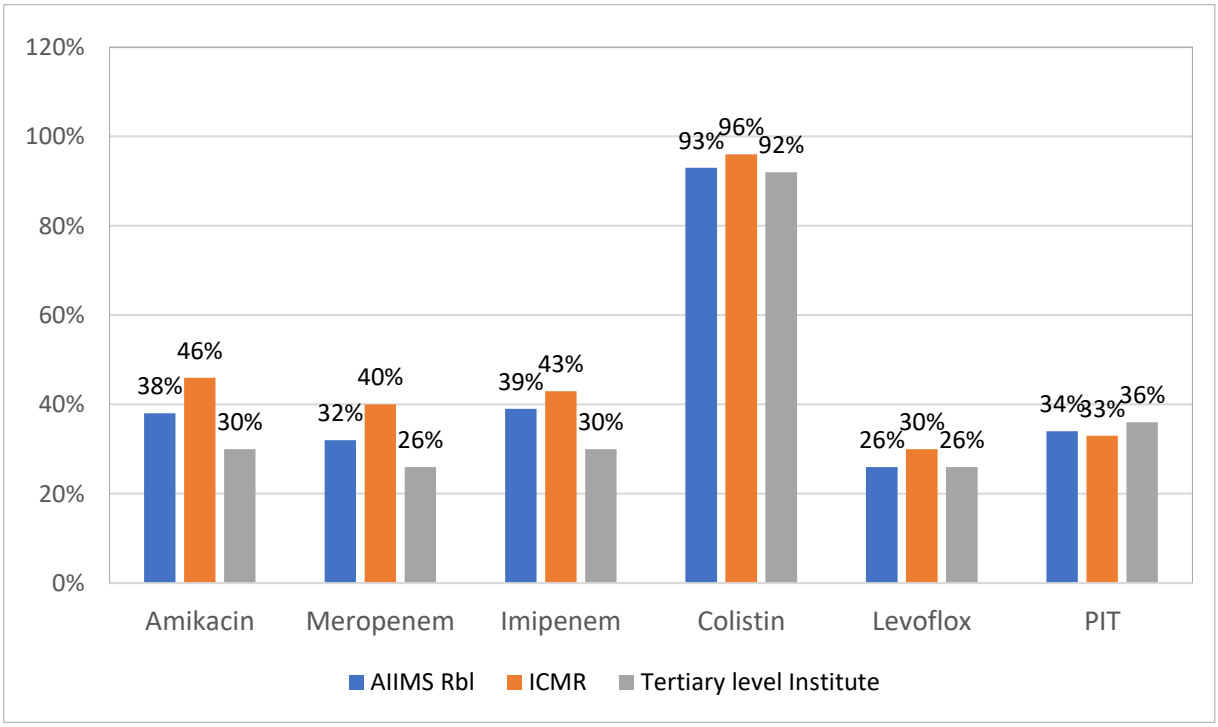

Fig 1: ***Escherichia coli:*** **Sensitivity rates to routine first line drugs.**

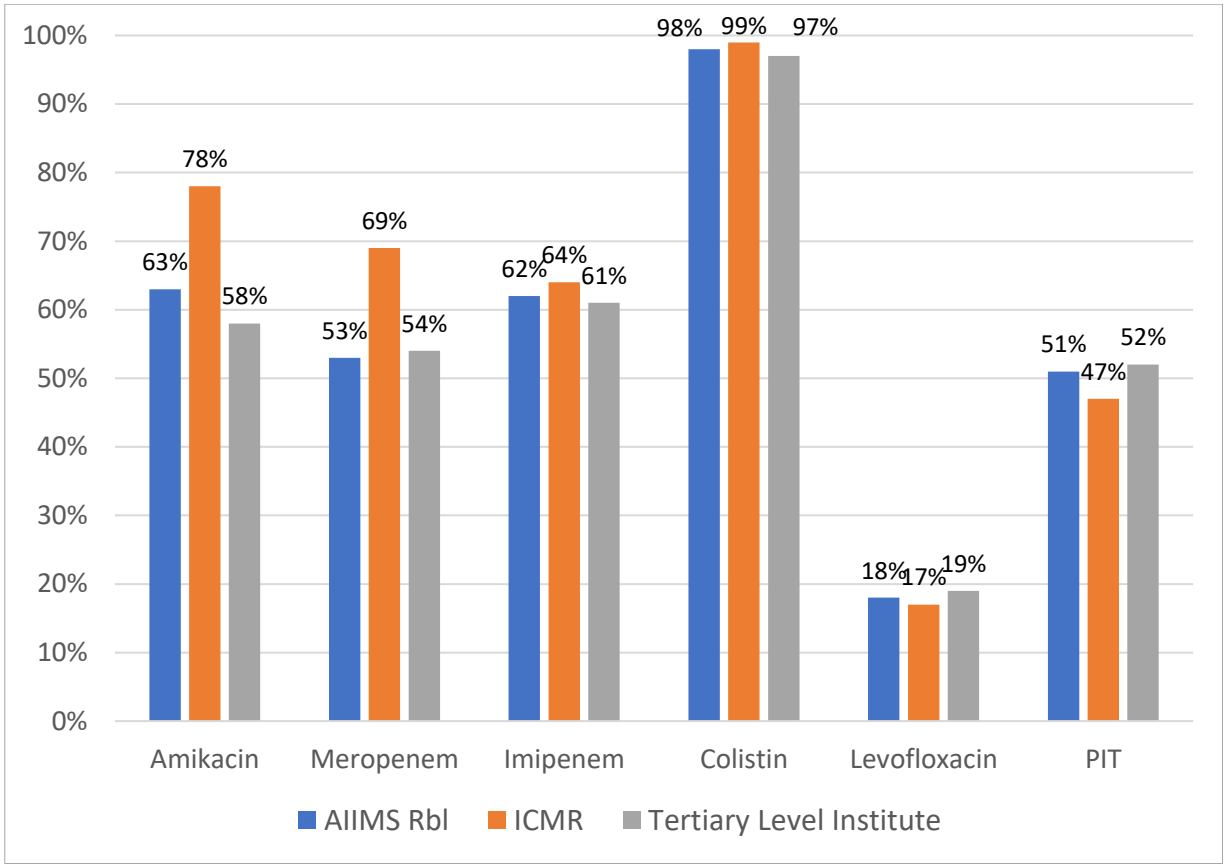

Fig 2: *Klebsiella pneumoniae:* Sensitivity rates to routine first line drugs.

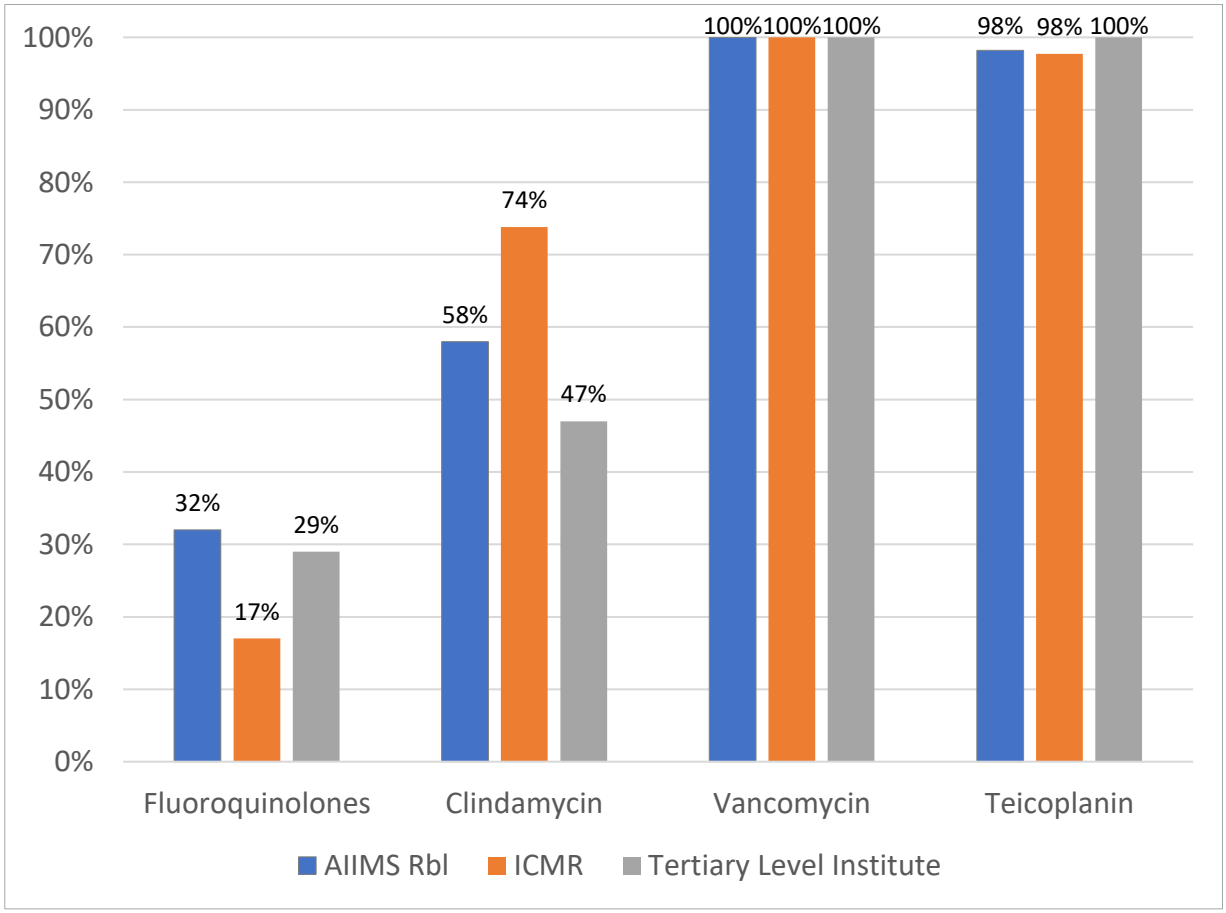

Fig 3*:* Staphylococcus aureus: Sensitivity rates to routine first line drugs.

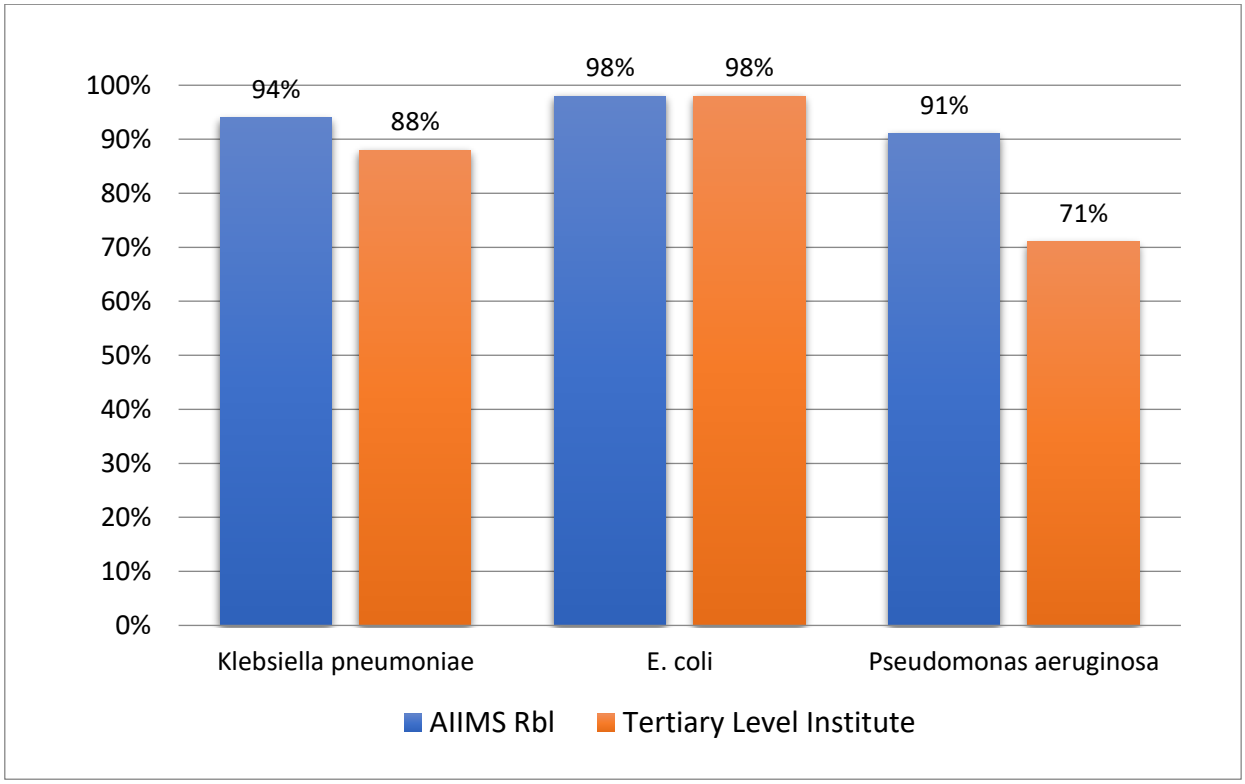

Fig 4: Fosfomycin: Second line sensitivity to various isolates

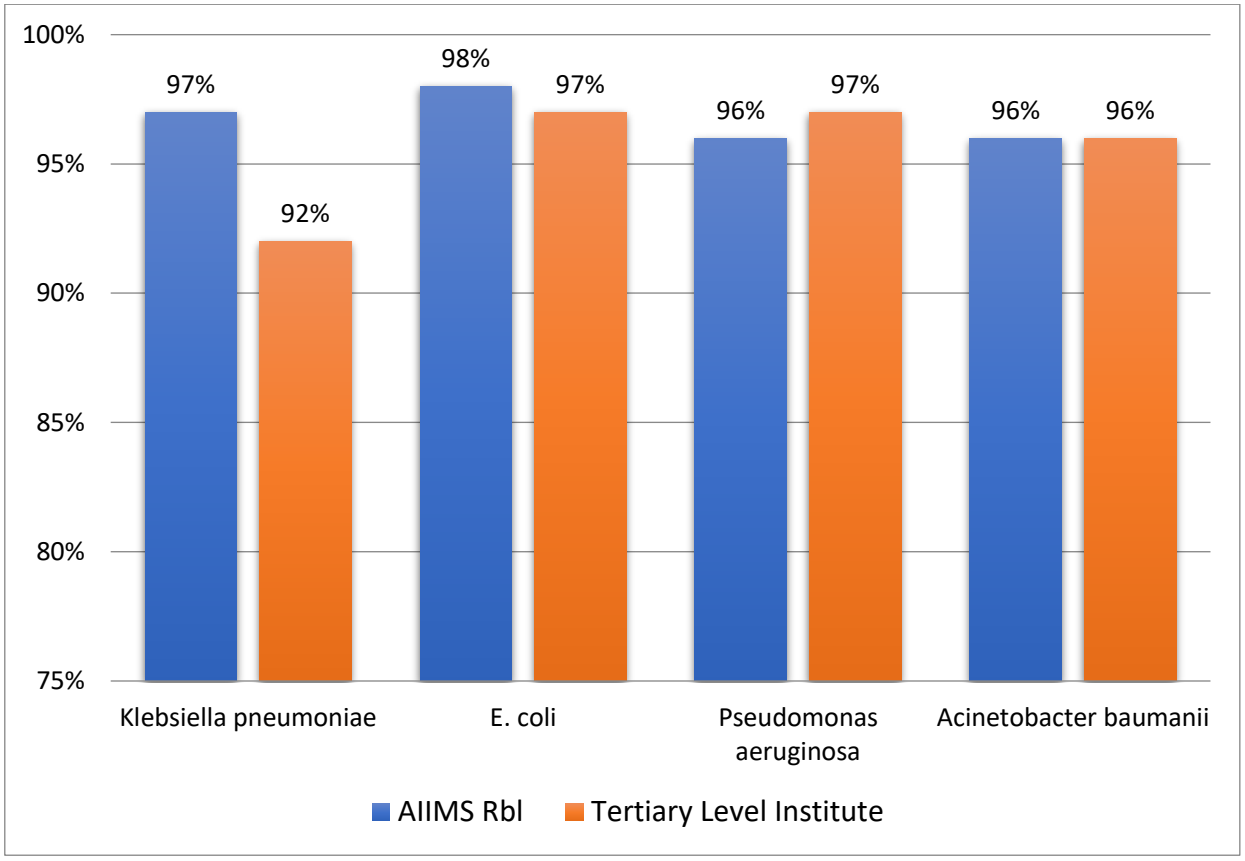

Fig 5: Colistin: Second line sensitivity to various isolates

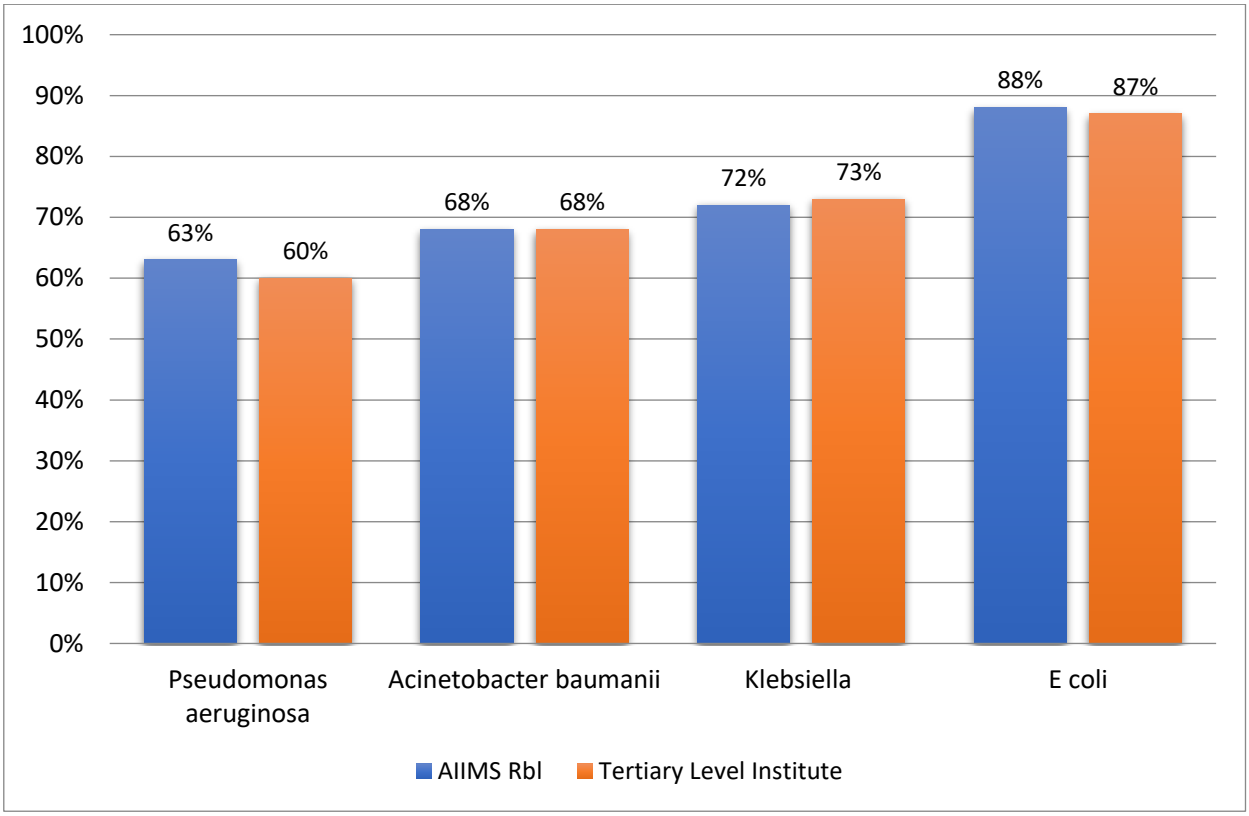

Fig 6: Minocycline: Second line sensitivity to various isolates

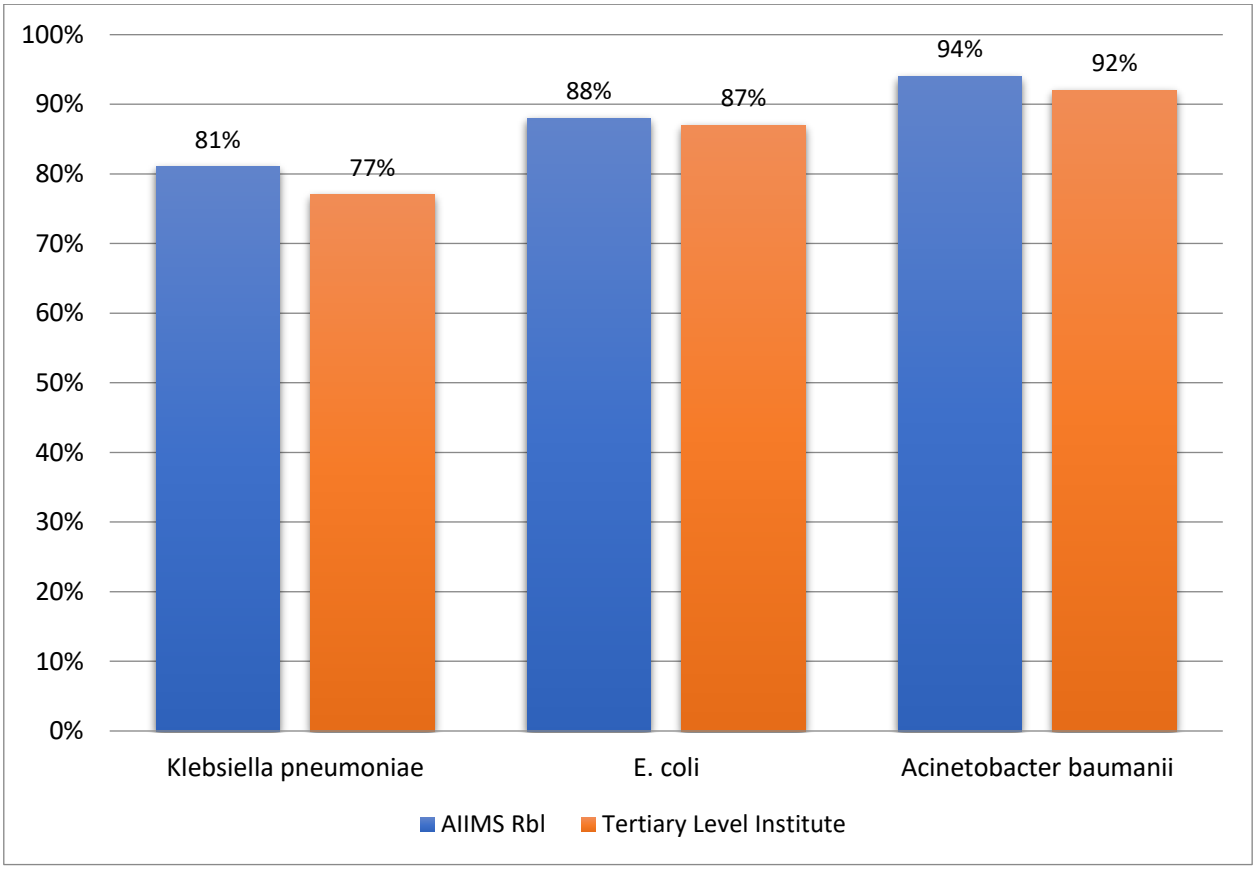

Fig 7: Tigecycline: Second line sensitivity to various isolates

Discussion

This study provides an elaborately made antibiogram profile of approximately two years from the diagnostic microbiology laboratory of a newly established tertiary level institute catering to the needs of thousands of local populations. This was the initial step of analysis of our Institute's antibiogram using the appropriate CLSI and EUCAST guidelines with the vision to incorporate it widely in the prescription of empirical therapy. The analysis has also shown that despite the increasing resistance to some antimicrobials, list of WHO access antimicrobials remains appropriate for our hospital setting.

The analysed antibiogram suggests that urinary tract (UTIs), respiratory and pyogenic infections were the most common reasons for ordering culture and sensitivity tests in our setting. One reason for this observation can be the ease of sample collection for these infections as compared to CSF and body fluids which require invasive procedures. Physicians treating the meningitis in paediatric age group usually tend to adopt the empirical therapy in such cases and also consider viral aetiologies often in such cases.

In our study; the predominant isolates were Gram-negative as compared to the gram-positive ones. This finding was in concordance with similar studies from various parts of the world namely; Ethiopia, India and China [15-17]. The isolation of gram-negative isolates in predominance can be justified by many ways. First, being the wide spread prevalence of these organisms in the hospital settings. Second is their non-fastidious nature and simple nutritional requirements for growth. Lastly, is the hardy nature of these organisms which resists their killing by normal disinfectants and chemicals.

Speaking of the sensitivity pattern of the Gram-negative isolates of the study; they showed a lower sensitivity to amikacin, carbapenems and colistin as compared to the ICMR data. This might be related to the easy availability as over the counter medications and irrational use of these drugs in this study area. Similar to our findings, Gram-negative isolates from a study in Ghana showed 94.4% resistance to ampicillin. However, other study by Debre Markos, Ethiopia demonstrated the rates of resistance to penicillin (71%), ampicillin (71%), amoxicillin (62.9%), cotrimoxazole (58.1%) and tetracycline (64.6) [18-20]. The possible explanation to the variations in the findings could be the differences in local population of the area studied, sample size, prevalence of isolates, etc.

The predominant isolates in our study i.e. *E.coli* and *Klebsiella* spp. were resistant to the cephalosporins, aminoglycosides, etc This reflected that the infection by these multidrug resistant organisms isolated from different body sites can be a cause of worry in this particular study area. However, the sensitivity to the higher order of second line antibiotics like Fosfomycin, colistin, Tigecycline and Minocycline was still high and not a major concern. This calls for a judicious use of the antibiotics as the near future may see resistance to these higher antibiotics too, as is seen in some of the developed countries. Majority of the isolates, 88% were single or multi drug resistant in the present study. This finding was very similar to a study done in Nepal (92.1%) and Debre Markos, Ethiopia (91.4%) and Indonesia [21-23].

On analysis of our antibiogram for the year wise trends in MDR isolates (2021-22 vs 2022-23), we found 56 % cases of MRSA in 2021-22 as compared to 54 % in 2022-23. This was in concordance to the study from Dessie, Ethiopia, and Kabul, Afghanistan (91.4%) [24-26]. Similarly, carbapenem resistant Acinetobacter species were isolated as 77% and 81% in 2021-22 and 2022-23 respectively; Colistin resistant Klebsiella species as 7% vs 9%, and Carbapenem resistant *Pseudomonas aeruginosa* as 40% vs 47%.Intrinsic resistance is noted in some isolates for a variety of antimicrobials. Some of the examples are: a) ***Burkholderia***: colistin, Fosfomycin, ticarcillin, ampicillin. b) ***Stenotrophomonas***: carbapenems, aminoglycosides, ticarcillin, ampicillin, aztreonam.c) ***Pseudomonas***: tigecycline, ertapenem. d) ***Proteus***: colistin, nitrofurantoin

In Carbapenem resistant *Pseudomonas aeruginosa*, usually an MIC of up to eight was seen with meropenem; however, imipenem as a monotherapy proved to be much more efficacious. The future lies in using the carbapenem sparing drugs for decreasing the trends of increasing resistance in MDR pseudomonas and Enterobacteriaceae family. One such drug is Ceftazidime-avibactam which was FDA approved in 2015 and is active against ESBL, amp C, OXA producing MDR Enterobacteriaceae and Pseudomonas species. It is not particularly active against MBL producing bacteria [27-28]. Another boon to these group of antibiotics is the discovery of Ceftriaxone-sulbactam-EDTA (ELORES). It is a Combination of Betalactam+ betalactamase + metal ion chelator; in which the primary drug is ceftriaxone. It has been cleared by Indian drug regulator and can be used for all infections (sepsis, pneumonia, intraabdominal infection, UTI) [29].

Despite the high rate of MRSA detection i.e; 56 % cases of MRSA in 2021-22 as compared to 54 % in 2022-23, our hospital setting showed improved sensitivity to vancomycin from 75.9 % in 2022 to 85% in 2023, as well as to most other first as well as second line antibiotics. We also reported a sensitivity rates of 99% and 95% of linezolid to MRSA and VRE isolates. The use of linezolid has an added benefit over currently used antibiotics as it is not natural but is synthetic in nature and there is no natural pool of resistance genes for it [30]. Ceftaroline has emerged as a new weapon in the limited armamentarium against gram positive organisms. It is a Fifth-generation cephalosporin and has been Approved by US FDA for skin and soft tissue infections, community acquired pneumonia especially by MRSA. It is currently being studied for sepsis and other infections [31,32].

According to a recent study during the COVID pandemic, the authors noted a dip in the overall sensitivity towards doxycycline and azithromycin. For doxycycline, the overall sensitivity was noted to be 46% in the year 2019-20 and 31% in the year 2020-21, whereas for erythromycin, the sensitivity was seen as 39% in 2019-20 and dropped down to 26% in 2020-21. This finding clearly indicates the increasing rates of antibiotic resistance in a developing country such as India during these COVID times [33]. The easy availability of these drugs as over the counter medications ad irrational use are the major factors for this resistance patterns.

The strength of this study lies in the fact that all antibiogram data available during the study period in our newly established setting was compared and analysed with the data available from ICMR as well as an established tertiary care institute. This helped in realistic comparison as well as practical applicability in the local population of our antibiogram data.

Limitation of the Study

This study may not represent the general population of the district or state as it was done in a newly established tertiary level institute. The study focussed on the routine antibiotics prescribed in the institute, not the other antibiotics which might be used rampantly in the local population of the study area. Hence, it may not truly represent the resistance pattern prevailing in the local study area.

Relevance and expected outcome: Antibiotic policy along with local antibiogram is the stepping stone towards accreditation of any hospital setting and ensures reliability as well as accuracy of results for better patient care. The local antibiogram provides a guide to the clinicians and helps them choose the best empirical antimicrobial treatment according to the local antibiogram in the event when microbiology culture and susceptibility results are pending. In the wider perspective, it will pave way for the implementation of antimicrobial stewardship program in the Institute and will be beneficial in bringing the rates of AMR under control.

Conflicts of Interest

None

Funding

None

Author's contribution

S.S. performed literature search, data analysis and first draft of the manuscript and figures.SI, SG contributed with the final draft of the manuscript and editing. CS contributed with antibiogram data of tertiary level institute. NKS and RV contributed with samples for processing for the study.

Acknowledgement

None

References

[1] American Thoracic Society. Guidelines for the initial management of adults with community-acquired pneumonia: Diagnosis, assessment of severity, and initial antimicrobial therapy. Am J Resp Crit Care Med. 2001, 163: 1730-1754.

[2] Naylor NR, Atun R, Zhu N, et al. Estimating the burden of antimicrobial resistance: a systematic literature review. *Antimicrob Resist Infect Control*. 2018;7(1):58. doi:10.1186/s13756-018-0336-y2.

[3] Antimicrobial Resistance Collaborators. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet; 399(10325): P629-655. DOI: https://doi.org/10.1016/S0140-6736(21)02724-0

[4] Aftab F Antibiotics as controlled medicines; 2016 [cited September 21, 2020]. Available from: https://www.duo.uio.no/han dle/10852/55030. Accessed May 20, 2021.3.

[5] Tanwar J, Das S, Fatima Z, et al. Multidrug resistance: an emerging crisis. *Interdiscip Perspect Infect Dis*. 2014;2014:2014. doi:10.1155/ 2014/5413404.

[6] Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. *Pharm Ther*. 2015;40(4):277.

[7] WHO. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2021; WHO: Geneva, Switzerland, 2021.

[8] Elton, L.; Thomason, M.J.; Tembo, J.; Velavan, T.P.; Pallerla, S.R.; Arruda, L.B.; Vairo, F.;Montaldo, C.; Ntoumi, F.; Hamid, M.M.A.; et al.Antimicrobial resistance preparedness in sub-Saharan African countries. Antimicrob. Resist. Infect. Control. **2020**, 9, 145.

[9] World Health Organization. Model List of Essential Medicines; WHO: Geneva, Switzerland, 2021.

[10] Hindler JA, Barton M, Erdman SM, et al. CLSI document M39-A4 Analysis and Presentation of Cumulative Antimicrobial Susceptibility Testing Data: Approved Guideline. 4th ed., Wayne, Penn: Clinical and Laboratory Standards Institute; 2014.

[11] Collee JG, Marr W. Specimen collection, culture containers and media. Mackie and Mac Carthey practical medical microbiology. 14th ed., New York: Churchill Living Stone; 1996. p. 95.

[12] Cheesbrough M. Part 2 District Laboratory Practice in Tropical Countries. 2nd ed., New York. USA: Cambridge University Press; 2006. p. 45-62. Part 2.

[13] Clinical and Laboratory Standards Institute (CLSI). CLSI supplement M100 Performance standards for antimicrobial susceptibility testing. 30th ed.., Wayne, PA: Clinical and Laboratory Standards Institute; 2020.

[14] The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 10.0, 2020. ⟨http:// www.eucast.org)."

[15] Mulu W, Abera B, Yimer M, et al. Bacterial agents and antibiotic resistance profiles of infections from different sites that occurred among patients at Debre Markos Referral Hospital, Ethiopia: a cross-sectional study. *BMC Res Notes*. 2017;10(1). doi:10.1186/ s13104-017-2584-y. 22.

[16] Lowy FD. Antimicrobial resistance: the example of Staphylococcus aureus. *J Clin Invest*. 2003;111(9):1265-1273. doi:10.1172/JCI18535 23.

[17] Magiorakos A-P, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect*. 2012;18(3):268-281. doi:10.1111/ j.1469-0691.2011.03570.x

[18] Demilie T, Beyene G, Melaku S, et al. Urinary bacterial profile and antibiotic susceptibility pattern among pregnant women in Northwest Ethiopia. *Ethiop J Health Sci*. 2012;22 (2):121-128.

[19] Samson OO, Anthony OE. Prevalence of multi-drug resistant staphylococcus aureus in clinical specimens obtained from patients attending the university of Benin Teaching Hospital, Benin City, Nigeria. *Prevalence.* 2013;3(5). 30.

[20] Ten Hove R-J, Tesfaye M, Ten Hove WF, et al. Profiling of antibiotic resistance of bacterial species recovered from routine clinical isolates in Ethiopia. *Ann Clin Microbiol Antimicrob*. 2017;16(1):46. doi:10.1186/s12941-017-0221-1 31.

[21] Ansari S, Nepal HP, Gautam R, et al. Threat of drug resistant Staphylococcus aureus to health in Nepal. *BMC Infect Dis*. 2014;14 (1):1-5. doi:10.1186/1471-2334-14-157 32. Jerry T, Queen AT, Tersagh I, et al.

[22] Antibiotic susceptibility pattern of gram-negative bacteria isolated from infected wound of patients in two health-care centers in Gboko Town. *J Clin Case Rep*. 2018;8 (1083):2. doi:10.4172/2165-7920.10001083 33.

[23] Amsalu A, Geto Z, Asegu D, Eshetie S. Antimicrobial resistance pattern of bacterial isolates from different clinical specimens in Southern Ethiopia: a three-year retrospective study. *Afr J Microbiol Res*. 2017;9(1):1-8. 34.

[24] Kumburu HHS, Mmbaga T, Alifrangis BT, et al. Patterns of infections, etiologic agents and antimicrobial resistance at a tertiary care hospital in northern Tanzania. *Trop Med Int Health*. 2017;22 (4):454-464. doi:10.1111/tmi.12836 35.

[25] Abejew AAD, Mekonnen AA, Gashaw A. Prevalence and antibiotic resistance pattern of urinary tract bacterial infections in Dessie area, North east Ethiopia. *BMC Res Notes*. 2014;7(1). 36.

[26] Naimi HM, Rasekh H, Noori AZ, et al. Determination of antimicrobial susceptibility patterns in Staphylococcus aureus strains recovered from patients at two main health facilities in Kabul, Afghanistan. *BMC Infect Dis*. 2017;17(737):844. doi:10.1186/s12879-017-2844-4.

[27] Hawkey PM, Warren RE, Livermore DM, McNulty CA, Enoch DA, Otter JA, et al. Treatment of infections caused by multidrug-resistant gram-negative bacteria: report of the British Society for Antimicrobial Chemotherapy/Healthcare Infection Society/British Infection Association joint working party. J Antimicrob Chemother 2018;73(suppl_3). iii2-78.

[28] Ramadan RA, Bedawy AM, Negm EM, Hassan TH, Ibrahim DA, ElSheikh SM, et al. Carbapenem-resistant Klebsiella pneumoniae among patients with ventilator-associated pneumonia: evaluation of antibiotic combinations and susceptibility to new antibiotics. Infect Drug Resist 2022;15:3537-48.

[29] Singh S, Sahu C, Patel SS, Singh A, Yaduvanshi N.A Comparative In Vitro Sensitivity Study of “Ceftriaxone-

Sulbactam-EDTA" and Various Antibiotics against Gram-negative Bacterial Isolates from Intensive Care Unit. Indian J Crit Care Med 2020;24(12):1213-1217.

[30] Stefani S, Bongiorno D, Mongelli G, Campanile F. Linezolid resistance in Staphylococci. Pharmaceuticals 2010;3(7):1988-2006.

[31] Hassoun A, Linden PK, Friedman B. Incidence, prevalence, and management of MRSA bacteremia across patient populations—a review of recent developments in MRSA management and treatment. Crit Care 2017;21(1):211.

[32] Li J, Zhao QH, Huang KC, Li ZQ, Zhang LY, Qin DY, et al. Linezolid versus. vancomycin in treatment of methicillin-resistant Staphylococcus aureus infections: a meta-analysis. Eur Rev Med Pharm Sci 2017;21(17):3974-9.

[33] Sahu C; Singh S; Pathak A; Patel S S; Ghoshal U; Singh U S. Trends of drug resistance to the commonly used antibiotics to combat the COVID-19 pandemic: Experience from a super-speciality institute of Northern India. Journal of Family Medicine and Primary Care 11(10):p 6255-6259, October 2022. | DOI: 10.4103/jfmpc.jfmpc_548_22