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Original Research Article

Stratified syndromic annual antibiogram for bloodstream infections - The need of the hour

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Abstract

Introduction: The routine antibiogram is a profile of antimicrobial susceptibilities which by using various parameters and stratifying the cumulative susceptibility help achieve enhanced or stratified antibiogram. Stratified antibiogram help guide empirical therapy for the selected patient groups.
Materials and Methods: The annual susceptibility data of blood culture isolates, where ≥30 isolates were available from January to December 2023 were compiled and the first isolates were filtered for various parameters such as syndromic, location, HA/CA and broad specialty in alignment to the standard CLSI M39 guidelines. The susceptibility was then calculated using a 'Clinical Microbiology Reporting software' and represented as S% - susceptibility percentage.
Result: The one-year study period, includes 2853 "first-isolates" that comprised of both gram-negative *bacilli* (GNB) and gram-positive *cocci* (GPC) blood culture pathogens. Analyzing syndromic antibiogram it is depicted that *E. coli* and *S. aureus* stand out as the major pathogen among GNB and GPC respectively. Enterobacterales (ENB) were found to have high resistance to third generation cephalosporins and *A. baumannii* complex had the least group of antimicrobial classes susceptible. The enhanced antibiogram of the major gram-negative pathogens from BSI showed that in general ICUs had more antimicrobial resistant (AMR) isolates, and HAI isolates were more resistant than CAI isolates. These differences were most evident in *K. pneumoniae* followed by *P. aeruginosa*.
Conclusion: Preparation of a Multi-stratified antibiogram such as BSI ICU antibiogram or BSI medicine antibiogram will be of utmost help in guiding correct empirical antimicrobial decisions if significant isolate number can be obtained.

Keywords: Sepsis, Routine Antibiogram, Empirical therapy, Syndromic antibiogram, Stratified antibiogram, Susceptibility

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1. Introduction

In routine antibiogram, the antimicrobial susceptibility data of the whole healthcare facility are summarized periodically and presented as percentages of organisms susceptible to a set of antimicrobial agents. There may be marked variability in the antimicrobial susceptibility test (AST) rates across various parameters (e.g., ICU vs. non-ICU setting; medicine vs. surgery units) within the same facility. A single facility-specific or hospital-wide routine antibiogram may mask these differences. The antimicrobial policy based on such routine antibiogram cannot be applied for specific patient populations or infection types and may result in inappropriate use of antimicrobials for empirical therapy. Therefore, it is recommended to construct an enhanced antibiogram by stratifying the cumulative AST data to answer specific clinical questions or help guide empirical antimicrobial therapy in select patient populations or infection types.[1,2]

Enhanced antibiogram (also known as customized or stratified antibiogram) is defined as an antibiogram prepared by stratifying the cumulative antimicrobial susceptibility data (S%) using various parameters to answer specific clinical questions or to help in guiding empirical antimicrobial therapy in selected patient populations or infection types.[3] There are various parameters which can be stratified in an enhanced antibiogram— clinical specimen type and subtype wise (i.e., syndromic), patientcare location wise (ICU, ward, OPD), patientcare broad specialty department wise (medicine, surgical, paediatric, and oncology-transplant alliances), and HAI/CAI (community- and healthcare- associated infections) wise etc. Multiple parameters can also be stratified at the same time (e.g., urine isolates from ICU setting), such antibiogram is called as multi-stratified enhanced antibiogram.[4] After the desired stratification filters are applied, the data is extracted, and then the first-isolate filter is applied at the end to select the first-isolate per patient per analysis period.

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Such antibiograms will be very useful for deciding on empirical decisions on the selected subset of population, especially life-threatening conditions like bloodstream infections (BSIs) and/or sepsis. The treatment of sepsis is highly time-sensitive, and empirical antibiotics play a crucial role in managing the condition, especially in the early stages.[5,6] However, to the best of our knowledge, there is paucity of such analysis of antibiogram data on BSIs and or sepsis. Therefore, we have designed this study to prepare a multi-stratified enhanced syndromic antibiogram for BSIs, based on specialty, location and HA/CA.

2. Materials and Methods

This is an observational prospective study conducted in blood culture division of microbiology laboratory in a large-scale teaching hospital of South India from January-December 2023. In our setting, the cultures are usually ordered for all the patients with suspected infections, intended to start on empirical antimicrobial therapy. As it is a free-service hospital, there is no financial restriction to order the cultures in indicated cases.

2.1. AST method

The patients with suspected BSIs and/or sepsis from whom the blood cultures yielded pathogen and subjected to AST were included in the study. The ID of the organism was obtained using MALDI-TOF MS, which was followed by AST using VITEK2 automated AST system (BMX VITEK). in which four AST panels were mainly used—N405 for Enterobacterales, N406 for non-fermenters, P628 for *Staphylococcus* and *Enterococcus* and ST03 for β-hemolytic *Streptococcus* and *S. pneumonia.* The VITEK2 AST method was followed as per the manufacturer's instruction and clinical and laboratory standards institute (CLSI) M100 and M07.[7,8] The laboratory was following the quality control (QC) protocol of AST on a weekly basis, as per CLSI M07, as well as participating in an external quality assessment services (EQAS) program.

2.2. Data collection

The AST data were collected using '*Clinical Microbiology Reporting software'*, developed by JIPMER in collaboration with Ibhar Pvt. Ltd., which was routinely used by our institute for reporting of blood culture AST. The various parameters collected were—healthcare-associated infection or community-associated infection (HAI/CAI), location (ICU, ward, or outpatient), broad speciality (medicine alliance, surgery alliance, paediatric alliance, oncology alliance), subspeciality (e.g. neurology), age category (<1yr, 1-5yr, 6-18yr, 19-64yr and >65yr), gender (male, female), specimen type (the present study includes only blood culture specimen), organism isolated, antimicrobial agent tested and its result in terms of both minimum inhibitory concentration (MIC) and its interpretation i.e., susceptible (S), intermediate (I), susceptible dose dependent (SDD) or resistant (R).

2.3. Validation of AST data

The AST report was validated as per CLSI M39[9] and other standard guideline.[1] Erroneous AST data were excluded from analysis. Any suspicious AST data was reconfirmed before including in the antibiogram. However, the highly suspicious AST report (such as vancomycin I and R results for *S. aureus*) if any, was reidentified after purifying the culture and repeated the AST and then submitted to reference center for confirmation before inclusion into antibiogram.

2.4. Development and validation of antibiogram

The antibiogram was generated using JIPMER-Ibhar antibiogram software, developed as per the recommendations from CLSI M39.[9] For routine antibiogram, the '*All-isolate AST data'* was collected and subjected to the '*first-isolate filter'*, defined as first-isolate of a given species per patient per analysis period (e.g., one year in our study) irrespective of body site, (blood, in our study), AST profile, or other phenotypic characteristics (e.g., biotype). As the primary objective of the antibiogram in our study was to guide the clinical decision on empirical antimicrobial therapy, first-isolate methodology was adopted. This is because, the antibiogram prepared from the first-isolate of a given species per patient will truly represent the susceptibility profile of the organism causing initial infections; thus, considered as the best approach of isolate selection to guide empirical therapeutic decisions. For generating multi-stratified antibiogram, the desired stratification filters (such as location, HA/CA, broad specialty) were applied on the '*All-isolate AST data'*, the data was extracted, and then finally the '*first-isolate filter'* was applied at the end to select the first-isolate of a given species per patient per analysis period (e.g., one year in our study).

The antibiogram was expressed in terms of susceptibility (S%) percentage; S and SDD results of the first-isolate were taken for numerator, whereas any all the first-isolates tested and valid AST results are available for particular antibiotic were used as denominator data for calculating S% for that species-antibiotic combination. The antibiogram developed was validated as per CLSI M39 recommendations and any suspicious or outlier S% were reviewed before their inclusion into antibiogram.

3. Result

In the one-year study period, 3653 "all-isolates" data of pathogens isolated from blood culture were collected, out of which 2853 "first-isolates" data were included in the study, that comprised of 2173 gram-negative bacilli (GNB) and 680 gram-positive cocci (GPC) pathogens.

Table 1 depicts the syndromic antibiogram of major gram-negative pathogens for bloodstream infections (BSIs). *Escherichia (E.) coli* (669) was the most common gram-negative pathogen isolated, followed by *Klebsiella (K.) pneumoniae* (403), *Acinetobacter (A.) baumannii* complex (383), *Pseudomonas (P.) aeruginosa* (199), *Burkholderia cepacia* complex (140) and *Enterobacter (E.) cloacae* complex (96). Enterobacterales (ENB) were found to have high resistance to third generation cephalosporins[3GC], with *E. coli* the most resistant, followed by *Proteus (P.) mirabilis*, *K. pneumoniae* and *E. cloacae* complex. Among ENB, carbapenems has acceptable susceptibility % (S% ~80%) for *E. coli* and *E. cloacae* complex, but poor for *K. pneumoniae.* For *A. baumannii* complex, none of the antimicrobials except minocycline (63%), tigecycline (82%) and colistin (97%) had

acceptable S%. *Aeromonas* species had acceptable S% for all except Piperacillin tazobactam (57.1%). *Salmonella* had shown poor S% to fluoroquinolones (28%).

The enhanced antibiogram of the major gram-negative pathogens for BSIs has been illustrated in **Table 2**, where the stratification is done by broad specialty (medicine, surgery, pediatric and oncology-transplant alliances), location (ICU vs ward/IPDs) and HAI/CAI (community vs healthcare associated). The stratified ABG for GNBs had been presented for only the major pathogenic GNBs such as *E. coli*, *K. pneumoniae*, *A. baumannii* complex, *P. aeruginosa* and *E. cloacae* complex. In general, as expected, ICU isolates had more antimicrobial resistance (AMR) than IPDs, and HAI isolates had more AMR than CAIs. These differences were most evident in *K. pneumoniae* followed by *P. aeruginosa*.

Table 3 illustrates the syndromic antibiogram of major gram-positive pathogens for BSIs. *Staphylococcus aureus* (317) was the most frequent gram-positive pathogen isolated, followed by *Enterococcus faecium* (112), *β hemolytic Streptococcus* (86), *Enterococcus faecalis* (73) and *Streptococcus pneumoniae* (51). The coagulase-negative staphylococci (CoNS) whose pathogenicity could not be ascertained were regarded as skin colonizers/contaminants and were excluded from analysis. About 35% of *S. aureus* isolates were methicillin resistant (MRSA), while almost 95% of pathogenic CoNS isolates were MR- CoNS. Fluoroquinolones had poor S% (~30%) for *Staphylococcus.* Erythromycin had poor S% (57%) but clindamycin & cotrimoxazole had acceptable S% (78%) for *S. aureus.* Tetracycline had excellent S% (92%) for *S. aureus.* Among *E. faecium* isolates, almost 28% were vancomycin resistant, and 6% were linezolid resistant. Minocycline demonstrated below-par S% for *Enterococcus* in general (~60%). *S. pneumoniae* had shown higher resistance for erythromycin (26%), tetracycline (24%), cotrimoxazole (8%). Almost 10% *S. pneumoniae* were resistant to penicillin and ceftriaxone.

The enhanced antibiogram of the major gram-positive pathogens for BSIs such as *S. aureus*, *E. faecium* and *E. faecalis* stratified by broad specialty, location and HA/CA has been illustrated in **Table 4**. The AMR pattern was almost comparable in ICUs vs IPDs as well as HAIs vs CAIs for *S. aureus* and *Enterococcus*.

In all the tables (**Table 1**, **Table 2**, **Table 3**, **Table 4**), only those organism species, where ≥30 isolates were available are depicted. The intrinsic resistant (IR) antibiotics, antibiotics for which no clinical breakpoint (NBP) is available, antimicrobials which are not tested (NT) or not reported (NR) in the concerned microbiology laboratory were abbreviated accordingly against the respective organism species in the tables.

4. Discussion

Preparation of regular antibiogram for a healthcare facility is a crucial responsibility of the clinical microbiologists. However, preparing annual routine antibiogram may not be very useful in terms of deciding initial empirical therapy for patients. Various stratified or enhanced antibiograms such as clinical specimen specific antibiogram (i.e., syndromic antibiogram), patientcare location-specific and treating department- specific antibiogram etc. are critical to be generated. On literature review on PubMed, there was paucity of literature on the search "syndromic antibiogram" as well as "stratified antibiogram". Among them, the majority of the literature were related to preparation of weighted incidence syndromic combination antibiograms (WISCA). Among all the infective syndromes, Bloodstream infections and/or sepsis are the most critical for which immediate empirical antimicrobial therapy needs to be initiated, which requires the preparation of a stratified syndromic antibiogram specific for bloodstream infections and/or sepsis or blood culture-specific antibiogram in true sense.

4.1. Syndromic antibiogram

Through this study, we developed stratified syndromic antibiogram for bloodstream infections and/or sepsis, which was further stratified by patientcare broad specialty departments, patientcare location/area type and community or healthcare associations (HA/CA).[4] Syndromic antibiogram was prepared from AST data on isolates recovered from select specimen types (e.g. blood culture in present study), and hence it can guide to take empirical decisions for BSIs and/or sepsis cases in a much better way than the routine antibiogram.[10]

4.2. Speciality antibiogram

As the patient profile admitted to various specialties or clinical services are dissimilar, there may be differences in the antimicrobial resistance pattern between various specialties. Therefore, a speciality-specific antibiogram gives accurate information about the susceptibility rate of organisms pertaining to the patients from that particular speciality.[11] From a clinician's perspective, this is an extremely useful antibiogram. In our study, the stratification was based on broad speciality— medicine, surgery, paediatric, and oncology/transplant alliances. Further stratification based on individual specialities under each of the broad specialities was not analysed because of less sample size. The AMR pattern varies among various specialities and also among different organism groups with no specific trend. This necessitates the generation of speciality specific antibiogram for a healthcare facility. In general, we found higher AMR rates in surgery alliance speciality and oncology-transplant alliance speciality.[12]

4.3. Location-specific antibiogram

Location-specific antibiogram, also called a nursing unit- or site-of-care-specific antibiogram may be helpful in the development of empirical antimicrobial treatment algorithms for patients with infections in that particular unit or site of care—e.g., sepsis treatment algorithms for patients in the ICU.[13] The AST pattern of organisms from ICU settings differs considerably from inpatient (IPDs), or outpatient (OPDs) setting. In our study, we observed that ICUs had higher AMR rates for majority of organism groups and antimicrobial agents, but we also found alarmingly high AMR rates in IPDs also, which pointed out the need of strong AMR containment and antimicrobial stewardship activities in IPDs as well as ICUs.

Table 1: Syndromic antibiogram of major gram-negative pathogens for bloodstream infections and/or sepsis

Antimicrobial Classes		**Cephalosporins**			**β-lactam combination agents**		**Carbapenems**		**Aminoglycosides**		**Quinolones**	**Folate antagonists**	**Tetracyclines**	**Glycylcyclines**	**Polymyxins**
		2nd Gen.	**3rd Gen.**	**4th Gen.**											
Antimicrobial agents / **Organism groups**	**No. of first isolates**	**Cefuroxime**	**Ceftriaxone (ENB) or Ceftazidime (NFGNBs)**	**Cefepime**	**Piperacillin tazobactam**	**Cefoperazone sulbactam**	**Meropenem**	**Imipenem**	**Gentamicin**	**Amikacin**	**Ciprofloxacin (ENB) or Levofloxacin(NFGNBs)**	**Cotrimoxazole**	**Minocycline**	**Tigecycline**	**Colistin**
Escherichia coli	669	13.8	18	30.3	66.5	75.5	79.5	80.4	59	81	4.2	35	89.5	99.8	98.8
Klebsiella pneumoniae	403	24.6	27.4	34.3	38.8	49.6	51	51.6	52.4	53.6	26.4	44	62.1	79.1	97.7
*Acinetobacter baumannii**	383	IR	16.5	15.7	16.7	23.8	17.5	17.1	19.4	18.8	17.5	27	63	81.8	97.6
Pseudomonas aeruginosa	199	IR	72.4	73.1	70.4	70.9	76.4	77.2	70.7	74.9	60.7	IR	IR	IR	97.9
Burkholderia cepacia complex	140	IR	94.3	NBP	IR	IR	95.7	NBP	IR	IR	73.6	98	95.7	NBP	IR
Enterobacter cloacae complex	96	36.6	47.3	62.8	64.6	83.2	84.2	79.8	72.9	86.5	55.2	76	86.8	96.8	93.5
Genus *Salmonella*	85	NBP	100	NBP	NBP	NBP	100	100	NBP	NBP	28.2	100	NBP	NBP	NBP
Stenotrophomonas maltophilia	75	IR	NBP	NBP	IR	IR	IR	IR	IR	IR	95.1	90	100	NBP	NBP
Elizabethkingia anopheles	33	IR	IR	IR	0	37.1	IR	IR	11.4	0.1	71.4	58	97.1	NBP	NBP
Proteus mirabilis	30	21.4	25	42.9	79.3	62.1	42.9	79.3	41.4	55.2	20.7	28	IR	IR	IR
Aeromonas spp.	30	70.4	75.9	88.5	57.1	89.7	63	46.4	96.4	96.7	86.7	82	NBP	NBP	NBP
Burkholderia pseudomallei	30	IR	88	NBP	NBP	NBP	100	NBP	IR	IR	NBP	88	NBP	NBP	IR

NBP, No Breakpoint available; IR, Intrinsic Resistant; gen., generation; **Acinetobacter baumannii* complex; ENB, Enterobacterales; NFGNB, nonfermenting gram-negative bacilli

Table 2: Enhanced antibiogram of major gram-negative pathogens for bloodstream infections stratified by broad specialty, location and HA/CA

Antimicrobial Classes		**Cephalosporins**			**β-lactam combination agents**		**Carbapenems**		**Aminoglyco-sides**		**Quinolones**	**Folate antagonists**	**Tetracyclines**	**Glycylcycline**	**Polymyxins**
Antimicrobial agents/ Organism groups	**No. of 1st isolates**	**Cefuroxime**	**Ceftriaxone (ENB), or Ceftazidime (NF-GNBs)**	**Cefepime**	**Piperacillin tazobactam**	**Cefoperazone sulbactam**	**Meropenem**	**Imipenem**	**Gentamicin**	**Amikacin**	**Ciprofloxacin (ENB) or Levofloxacin(NFGNBs)**	**Cotrimoxazole**	**Minocycline**	**Tigecycline**	**Colistin**
E. coli	669	13.8	18	30.3	66.5	75.5	79.5	80.4	59	81	4.2	35	89.5	99.8	98.8
Medicine alliance	442	14.1	19.1	30	45.2	56.4	57.5	58.1	54.5	58.6	32	36.8	91.2	100	98.8
Surgery alliance	149	13	15	33	63	78	77	78	69	87	5.4	33.6	85	99	98
Pediatrics alliance	58	20.7	24.1	32.8	67.2	69	72.4	72.4	53.4	69	1.7	32.8	92.5	100	100
Onco-transplant*	38	8.1	10.8	22	58	68	74	71	71	76	27	26	85	100	100
ICUs	223	9	11.5	21	54	62	66	68	54	76	0.1	25.4	88	100	99.2
IPDs	441	14.1	18	32.2	66.5	76	79.1	80.5	58.6	82.6	4.3	35.2	89.3	100	89.3
Healthcare (HAIs)	329	12	15.1	27.5	61.6	68	73	72.9	58	76	2.7	32.4	96.8	99.6	98
Community (CAIs)	340	13.7	19.5	31	71.3	82.4	85.2	86.8	58.5	83.5	5.6	36.9	95.2	100	99.4
K. pneumoniae	403	24.6	27.4	34.3	38.8	49.6	51	51.6	52.4	53.6	26.4	44	62.1	79.1	97.7
Medicine alliance	220	30.7	33.5	41	45.6	56.4	58.3	58.1	54.5	58.9	32	50.2	69.7	84.9	97.7
Surgery alliance	108	13	16	21	22	29	32	32	46	36	11	33.3	47	67	97
Pediatrics alliance	50	10	10	16	32	54	56	57.1	44	60	16	28	61.9	80	97.9
Onco-transplant *	30	39	46.4	59	55	62	62	62	66	66	52	52	68	83	100
ICUs	166	11	13.2	17	24	35	39	38	40	40	15	31.9	47	68	94.8
IPDs	233	24.4	26.6	33.3	35.6	47.9	49	49.7	52.6	53.6	25.9	40.4	60.5	79.9	98.9
Healthcare (HAIs)	259	14	14	16	21.3	29.6	33.7	33	36	35	13	26.2	60	74.1	96.5
Community (CAIs)	144	41.1	45.1	57.3	61.5	72.9	73.2	73.4	68.8	75.7	45.8	65.3	87	91	99.3
A. baumannii	383	IR	16.5	15.7	16.7	23.8	17.5	17.1	19.4	18.8	17.5	27	63	81.8	97.6
Medicine alliance	201	IR	17.8	15.8	17.1	24.8	18.1	17.3	20	19.5	17.2	25.7	59.1	82.2	98.1
Surgery alliance	123	IR	7.3	6.5	7.3	15	7.3	7.3	9.8	11	9.8	18.2	61	76	100

Pediatrics alliance	36	IR	33.3	38.9	38.9	38.9	41.7	41.7	41.7	36.1	38.9	61.1	88.9	88.9	88.2
Onco-transplant*	31	IR	39	39	39	46	39	39	39	39	39	39	77	92	92
ICUs	172	IR	13	11	13	22	13	13	15	13	13	23.7	66	83	98.6
IPDs	211	IR	16.3	16.2	16.8	23	18.3	16.8	21.1	20.9	18.4	28	59.3	81	96.3
Healthcare (HAIs)	299	IR	12	11.9	13	18.2	11.7	12	15	13	14	23	53.6	72.3	98
Community (CAIs)	84	IR	28.9	28.6	30.1	42.9	34.2	33.3	34.2	36.9	32.1	44.6	75.6	87.3	95.1
P. aeruginosa	199	IR	72.4	73.1	70.4	70.9	76.4	77.2	70.7	74.9	60.7	IR	IR	IR	97.9
Medicine alliance	93	IR	80.8	82.7	80.8	80.8	86.5	85.3	80	81.7	68.3	IR	IR	IR	98.1
Surgery alliance	47	IR	44.7	39.1	38.3	38.3	44.7	50	40	42.6	34	IR	IR	IR	97.8
Pediatrics alliance	30	IR	85.7	92.9	85.7	89.3	92.9	89.3	100	100	75	IR	IR	IR	100
Onco-transplant*	31	IR	75	74	74	70	75	79	67	80	65	IR	IR	IR	95
ICUs	85	IR	60	61	55	56.7	61.7	67.2	68.8	68.3	50.8	IR	IR	IR	100
IPDs	110	IR	74.4	75.6	73.3	75.6	78.9	79.3	72.7	75.6	64.8	IR	IR	IR	97.7
Healthcare (HAIs)	134	IR	62	60.4	58.5	58.5	68.9	70.9	70	66	56	IR	IR	IR	69.1
Community (CAIs)	65	IR	83.1	89.1	84.6	86.2	87.7	85.7	72	86.2	67.7	IR	IR	IR	100
***E. cloacae* complex^**	96	36.6	47.3	62.8	64.6	83.2	84.2	79.8	72.9	86.5	55.2	76	86.8	96.8	93.5
Medicine alliance	60	41.2	51.5	69.1	71.4	89.9	91.3	85.9	75.7	90	58.6	84.3	86.2	97.1	93.9
Surgery alliance	31	50	100	100	58.6	100	100	100	100	100	100	100	100	100	100
ICUs	40	25	47.6	54.5	65.2	77.3	77.3	75	73.9	78.9	47.8	65.2	88.9	100	90.5
IPDs (wards)	55	37.5	44.4	60.7	58.9	82.1	85.7	78.8	67.9	87.5	55.4	75	85.7	94.6	92.6
Healthcare (HAIs)	56	29	35.7	48.8	54.6	72.7	72.7	70.7	60	80	44	68.9	87.5	95.4	90.5
Community (CAIs)	40	32.5	46.2	65	69.2	87.5	89.7	81.6	77.5	85	55	82	91.7	100	94.9

NBP, No Breakpoint available; IR, Intrinsic Resistant; gen., generation; *# Acinetobacter baumannii* Complex; * Onco-transplant alliance; ICU, Intensive care unit; IPD, inpatient department (wards); ^Pediatrics alliance and Onco-transplant alliance for *Enterobacter cloacae* complex has not been analyzed because of les then 30 sample size.

Table 3: Syndromic antibiogram of major gram-positive pathogens for bloodstream infections and/or sepsis

Antimicrobial Classes		**Anti- Staph Penicillins**	**Penicillins**	**3rd Gen. Cephems**	**Macrolides**	**Lincosamides**	**Aminoglycosides**	**Fluoroquinolones**	**Folate antagonists**	**Tetracyclines**	**Glycylcyclines**	**Glycopeptides**	**Oxazolidinones**	**Phenicols**	**Lipopeptides**	**Rifamycins**					
Antimicrobial agents/ Organism groups	**No. of 1st isolates**	**Oxacillin/Cefoxitin**	**Penicillin**	**Ampicillin**	**Ceftriaxone**	**Erythromycin**	**Clindamycin**	**Gentamicin**	**High level Gentamicin**	**Ciprofloxacin**	**Levofloxacin**	**Cotrimoxazole**	**Tetracycline**	**Minocycline**	**Tigecycline**	**Vancomycin**	**Teicoplanin**	**Linezolid**	**Chloramphenicol**	**Daptomycin**	**Rifampicin**
Staphylococcus aureus	317	65	NT	NBP	SP1	57	78	74	NBP	28	35	78	92	NT	100	100	100	100	NT	100	100
CoNS	41	5	NT	NBP	SP1	32	64	50	NBP	29	29	46	44	NT	100	100	100	100	NT	100	88
Enterococcus faecium	112	NBP	5.4	5.4	IR	IR	IR	IR	27	NR	NR	IR	NR	57	100	72	92	94	NT	NT	NT
Enterococcus faecalis	73	NBP	85.7	91	IR	IR	IR	IR	43	NR	NR	IR	NR	64	100	100	100	100	NT	74	NT
β hemolytic Streptococci	86	NBP	100	100	100	52	81	NBP	NBP	NBP	84	NBP	35	NBP	100	100	100	100	65	NT	100
Streptococcus pneumoniae	51	NBP	89.8 (NM) 32.4 (M)	NBP	89.8 (NM) 69.6 (M)	26	60	NBP	NBP	NBP	94	7.8	24	NBP	100	100	100	100	92	NBP	98

* *CoNS*, Coagulase negative *Staphylococcus*; IR, Intrinsic Resistant; NT, Not tested; NR, Not Reported; NBP, No Breakpoint available; SP1, Predicted susceptibility of oxacillin to ceftriaxone; M, Meningitis breakpoint; NM, Non-meningitis breakpoint

Table 4: Enhanced antibiogram of major gram-positive pathogens for bloodstream infections stratified by broad specialty, location and HA/CA

Antimicrobial Classes		**Anti- Staph. Penicillins**	**Penicillins**	**Aminoglycosides**	**Quinolones**	**Folate antagonists**	**Tetracyclines**	**Glycylcycline**	**Glycopeptides**	**Macrolides**	**Lincosamide**	**Oxazolidinones**					
Antimicrobial agents/ Organism groups	**No. of first isolates**	**Oxacillin/ Cefoxitin**	**Penicillin**	**Ampicillin**	**Gentamicin**	**High level Gentamicin**	**Ciprofloxacin**	**Levofloxacin**	**Cotrimoxazole**	**Tetracycline**	**Minocycline**	**Tigecycline**	**Vancomycin**	**Teicoplanin**	**Erythromycin**	**Clindamycin**	**Linezolid**
Staphylococcus aureus	317	65.3	NT	NBP	74.5	NBP	27.8	34.8	77.9	92	NT	100	100	100	56.8	78	100
Medicine alliance	258	67.6	NT	NBP	72.8	NBP	26.4	34.4	81.5	92	NT	100	100	100	58.1	78.4	100
Surgery alliance	44	52.3	NT	NBP	68	NBP	27.3	31.8	79.5	88	NT	100	100	100	54.5	80	100
Pediatrics alliance	34	66.7	NT	NBP	88.2	NBP	29.4	41.2	58.8	94	NT	100	100	100	52.9	80.6	100
Onco-transplant*	32	54	NT	NBP	85	NBP	31	31	62	100	NT	100	100	100	39	62	100
ICUs	81	63	NT	NBP	82.6	NBP	28.3	37	76.1	91.3	NT	100	100	100	54.3	81.8	100
IPDs (wards)	229	63.4	NT	NBP	70	NBP	29.9	36.1	79.4	91.2	NT	100	100	100	58.8	7.4	100
Healthcare (HAIs)	162	69	NT	NBP	76	NBP	30	37	80.8	92	NT	100	100	100	57	74	100
Community (CAIs)	155	65	NT	NBP	72.6	NBP	24.7	32.3	75.5	92.3	NT	100	100	100	55.5	76.9	100
Enterococcus faecium^	112	X	5.4	5.4	IR	27	NR	NR	IR	NR	57	100	72	92	IR	IR	94
Medicine alliance	71	NBP	5.3	5.3	IR	23.7	NR	NR	IR	NR	53.2	100	72.6	93.1	IR	IR	92
Surgery alliance	31	NBP	0	0	IR	36.8	NR	NR	IR	NR	83.8	100	78.9	100	IR	IR	94.7
ICUs	31	NBP	4.3	4.3	IR	21.7	NR	NR	IR	NR	56.2	100	66.7	93.3	IR	IR	100
IPDs (wards)	72	NBP	2.8	2.8	IR	23.6	NR	NR	IR	NR	57.8	100	72.5	92.9	IR	IR	94.4
Healthcare (HAIs)	82	NBP	1.6	1.6	IR	30	NR	NR	IR	NR	66.7	100	65.6	88.6	IR	IR	93.6
Community (CAIs)	30	NBP	13.3	10	IR	26.7	NR	NR	IR	NR	47.4	100	75.9	95.8	IR	IR	93.3
Enterococcus faecalis^	73	NBP	85.7	91	IR	43	NR	NR	IR	NR	64	100	100	100	IR	IR	100
Medicine alliance	41	NBP	88.5	88.7	IR	43.6	NR	NR	IR	NR	60.5	100	100	100	IR	IR	100
Surgery alliance	30	NBP	100	100	IR	30.8	NR	NR	IR	NR	72.7	100	100	100	IR	IR	100
ICUs	30	NBP	76.9	85.7	IR	33.3	NR	NR	IR	NR	66.7	100	100	100	IR	IR	100
IPDs (wards)	39	NBP	92.1	94.7	IR	48.7	NR	NR	IR	NR	66.7	100	100	100	IR	IR	100
Healthcare (HAIs)	42	NBP	93.6	96.8	IR	37	NR	NR	IR	NR	100	100	100	100	IR	IR	100
Community (CAIs)	31	NBP	75.9	85.7	IR	35.5	NR	NR	IR	NR	60.9	100	100	96.8	IR	IR	100

NBP, No Breakpoint available; IR, Intrinsic Resistant; NT, Not tested; NR, Not Reported for blood isolates; gen., generation; *# Acinetobacter baumannii* Complex; * Onco-transplant alliance; ICU, Intensive care unit; IPD, inpatient department (wards); ^Pediatrics alliance and Onco-transplant alliance for *Enterococcus faecium and Enterococcus faecalis* have not been analyzed because of less than 30 sample size.

4.4. HA/CA antibiogram

Antibiogram can be customized for healthcare-associated and community-associated infections. If the time gap between patient's admission and specimen collection is <48h, the isolate can be arbitrarily included under community-associated infection (CAI), whereas a time gap of ≥48h would categorize the isolate under healthcare-associated infections (HAI).[14,15] Collection of accurate data on patient's admission as well as sample collection (date and time) is a prerequisite to prepare this type of antibiogram. HA/CA antibiogram helps to understand the difference in the antimicrobial resistance pattern between the organisms recovered from HAIs and CAIs. Alarmingly high AMR was noticed even among CAIs in the current study which goes against the general notion that AMR is primarily restricted among healthcare setups. This necessitates the implementation of strong AMR containment and antimicrobial stewardship activities in community settings as well. However, one limitation of this HA/CA categorization was that the patients with frequent re-admissions or OPD follow-ups following long hospital stays might still be categorised as community-associated, which might be one of the reason for higher AMR rates in CAIs in the study.

4.5. Antibiogram (syndromic and stratified) for gram-negative pathogens

In our study, for both syndromic and stratified antibiogram, the decreasing order of susceptibility to β-lactam drugs to majority of GNBs was found to be carbapenems followed by β-lactam combination agents (BLBLIs) such as piperacillin-tazobactam (PTZ) and cefoperazone-sulbactam (CFS), followed by 4th gen. cephems (cefepime), 3rd gen. cephems (ceftriaxone for Enterobacterales, or ceftazidime for non-fermenters), and 2nd gen. cephems cefuroxime (for Enterobacterales). Differences in the S% of carbapenems such as meropenem, imipenem, and ertapenem were found to be <10%. Differences in the S% of BLBLIs such as PTZ and CFS were found to be <10%. Colistin (S%) was found to be >90% for all major gram-negative organism groups. Tigecycline(S%) was also observed to be >90% for all major gram-negative organism groups. Amikacin (S%) was found to be higher than that of gentamicin (S%) for all major gram-negative organism groups. Tigecycline (S%) was also found to be higher than that of minocycline (S%) for all major gram-negative organism groups.

4.6. Antibiogram (syndromic and stratified) for Gram-positive pathogens

In our study, for both syndromic and stratified antibiogram, doxycycline, cotrimoxazole and clindamycin were found to be acceptable empirical treatment options against coverage of *S. aureus* especially in hemodynamically stable and mild-to-moderate ill patients. Glycopeptides (i.e., vancomycin and teicoplanin) and linezolid had demonstrated 100% susceptibility for *S. aureus* and hence are more suited as empirical choices for hemodynamically unstable and/or severely ill patients requiring *S. aureus* coverage. MRSA (35%) and pathogenic MR-CoNS (95%) isolation rates was found to be alarmingly high in our study which needs attention and reduces the possibility to use anti-Staphylococcal penicillins as empirical choices. Even VRE rates were found to be high among *E. faecium* (28%). Linezolid and tigecycline seemed as the only available treatment options for such VRE isolates. We documented a high ceftriaxone resistance rate (10%) among *S. pneumoniae* which is a matter of great concern.

5. Conclusion

Preparation of routine antibiogram for a healthcare facility is not enough for appropriate patient management decisions. Every facility should prepare dedicated enhanced stratified antibiogram on a regular basis. Important stratifications required for antibiogram are specimen-specific (or syndromic) especially those for bloodstream infections and/or sepsis, patientcare location specific antibiogram, clearly separating ICUs from IPDs and OPDs, treating specialty specific (with minimum categorizing into major broad specialties if not into individual departments) and if possible, into HAIs vs CAIs. Multi-stratified antibiogram preparation such as BSI ICU antibiogram or BSI medicine antibiogram or BSI medicine ICU antibiogram is much more helpful in guiding correct empirical antimicrobial decisions if significant isolate number can be obtained.

6. Ethical Approval

Study was approved by Institute Ethical approval committee with ref. no. JIP/IEC/2021/256

7. Source of Funding

None.

8. Conflict of Interest

None.

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