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Formulation of In-Patient Hospital Antibiogram and Evaluation of the Burden of Antibiotic Resistance at a Tertiary Care Teaching Hospital in South India

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ABSTRACT

Antibiotic resistance has been a recognized reality since the dawn of the antibiotic era, but it is only in the last two decades that lethal, resistant strains have developed with worrying regularity. The "**ESKAPE**" (**E**nterococcus faecium, **S**taphylococcus aureus, **K**lebsiella pneumonia, **A**cinetobacter baumannii, **P**seudomonas aeruginosa, **E**nterobacter spp.) group of pathogens demands the most attention. Pharmacists, according to the American Society of Health-System Pharmacists (ASHP), have a responsibility to play a significant role in antimicrobial stewardship programs. To support antimicrobial stewardship, the present study aims to observe the local resistance patterns by formulating an annual cumulative antibiogram of in-patients along with an additional sub-analysis of the influence of age, gender, and location of bacterial isolates susceptibility to the commonly prescribed antibiotics. A retrospective, healthcare record-based, cross-sectional study was conducted after ethical approval at a tertiary–care teaching hospital in south India. We gathered data from the medical records of the inpatients satisfying the inclusion and exclusion criteria for the year 2020 from January 1, 2020, to December 31, 2020. A cumulative antibiogram was created using the software WHONET 2020 (Version 20.17.26) and statistical analysis was done using IBM SPSS Statistics software (Version 23). Chi-square was applied and a p-value of < 0.05 was considered significant. A total of 774 patients were included in which there was a higher male preponderance. Pus cultures were the highest, 295 (38.1 %) followed by Urine cultures, 206 (26.6 %), Sputum cultures, 116 (14.9 %), Blood cultures, 63 (8.1 %), Tracheal aspirates 37 (4.8 %) and Genital cultures, female 30 (4.0 %). Staphylococcus aureus (n = 234) 30.2 % was the most prevalent organism followed by Escherichia coli (n = 213) 27.5 %, Klebsiella spp., (n = 159) 20.5 % and Pseudomonas spp., (n = 144) 18.6 %. Antibiotic susceptibility patterns to bacterial isolates differed significantly by age, gender, and location among inpatients. The current study provides insight into the regional trend of antibiotic resistance. We recommend the formulation of stratified antibiograms. Our findings will aid in the establishment of antibiotic policy and the selection of empiric therapy options.

INTRODUCTION:

Antibiotics have completely transformed medical practice, enabling the treatment of diseases that were previously deadly and other medical breakthroughs such as cancer chemotherapy and organ transplants to be made. The use of antibiotics early in the treatment of infections has been shown to reduce morbidity and save lives, with a recent example being the use of antibiotics early in the treatment of sepsis. Inappropriate antibiotic use, on the other hand, leads to bacterial resistance development, hastening the establishment and spread of resistant germs and affecting treatment outcomes. Antibiotics, like all drugs, have major side effects, such as allergic responses and *Clostridium difficile* infection (CDI). Patients who are given antibiotics needlessly run the risk of major side effects with no clinical benefit.[1]Antimicrobial resistance (AMR) occurs when potentially hazardous bacteria evolve in such a way that the antibiotic's effectiveness is reduced or eliminated.[2]Although AMR is a prevalent problem, it is becoming more common as a result of incorrect antibiotic use and prescribing. Due to its quick onset and spread, AMR has become a global problem during the last few decades. Antibiotic overuse has also led to the rise of antibiotic resistance, which has become one of the most serious and rapidly spreading public health risks.[3] Antibiotic abuse, unlike other drugs, can spread resistant organisms, putting the health of patients who aren't even exposed to them at risk.[1]As a result of Multi-Drug Resistant clones' successful penetration and proliferation in nosocomial settings, AMR is becoming a growing problem not just in hospitals, but also in community-acquired diseases.[4] The "**ESKAPE**" (***E****nterococcus faecium*, ***S****taphylococcus aureus*, ***K****lebsiella pneumonia*, ***A****cinetobacter baumannii*, ***P****seudomonas aeruginosa*, ***E****nterobacter spp.*)group of pathogens, based on overall mortality and economic impact, demands the most attention, both clinically and in terms of research and development.[5-6] In 2008, Rice coined the word ESKAPE to describe a category of viruses that can evade drug biocidal action.[7]Antibiotic-resistant organisms infect more than two million individuals, according to the Centers for Disease Control and Prevention (CDC), resulting in around 23,000 fatalities each year.[1]

An increasing body of research shows that "Antibiotic Stewardship Programs (ASPs)," antibiotic-use improvement strategies based in hospitals, can both maximize infection therapy and reduce adverse effects associated with antibiotic use.[8] The Centers for Disease Control and Prevention (CDC) advised in 2014 that all hospitals develop an ASP with seven essential components. Some of the strategies within the fundamental elements include monitoring prescription patterns and resistance and providing local prescribing and resistance

information directly to health care practitioners. Although it is necessary to be flexible when designing such programs, and the details must be tailored to each institution, the cornerstone for a successful ASP is a collaborative effort between pharmacy, infectious disease specialists, and the clinical microbiology laboratory, as well as leadership support.[9]Antimicrobial stewardship in health systems is described in guidelines published by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America, which have been adopted by American Society of Health-system Pharmacists and other organizations, as well as the critical role that pharmacists with infectious disease training play in leading stewardship efforts. Antimicrobial stewardship and infection prevention and control responsibilities for pharmacists include advocating effective antimicrobial use, reducing illness transmission, and educating healthcare providers, patients, and the general public. Working with microbiology lab professionals to ensure that relevant microbial susceptibility tests on specific patients are reported as soon as possible, and cooperating with microbiology lab and infectious disease personnel to ensure that individual microbial susceptibility test findings are reported on time as well as hospital-wide and unit-specific microbial susceptibility data to prescribers. This can be accomplished by creating an antibiogram for the institution.[10]An antibiogram is the result of laboratory testing of an isolated bacterial strain's susceptibility to antibiotics over a set period, usually six to twelve months for a specific institution. The results of cumulative susceptibility are compiled into a summary table, often known as a cumulative antibiogram, or simply the antibiogram. The total number of bacterial isolates screened against a variety of antimicrobials is shown in a typical antibiogram.[11] In different parts of the world, disease resistance differs.[10]Because of the absence of uniformity in the preparation of hospital antibiograms, aggregate susceptibility data may be misinterpreted and misapplied when making empiric antibiotic recommendations. The absence of published data on the clinical application of institution-specific antibiogram data and the limitations associated with microbiologic reporting has hampered efforts to maximize their usage in clinical practice even more. The National Committee for Clinical Laboratory Standards (NCCLS) group released a document titled "Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data: Approved Guideline" to assist health care establishments (NCCLS M39-A).[12]because bacterial susceptibility patterns vary by region, each institution will have its antibiogram. As a result, antibiogram results from one facility cannot be used at another unless the facilities are near one another and/or share the majority of patients/residents. As a result, local resistance patterns must be understood to employ antimicrobials effectively.[11]The World Health

Organization (WHO) has set up a program to combat antibiotic resistance. The Antimicrobial Resistance Monitoring (ARM) Programme is what it's called. It is necessary to have reliable and freely accessible data on antimicrobial resistance to assist decision-making and take action at all levels, from local to global. To do all of this, the WHO developed WHONET, a free electronic format, Windows-based database software that was created for the management and analysis of microbiology data, with a particular focus on antimicrobial susceptibility test results analysis.[13-14]

Even though the antibiograms are meant to assist clinicians in empiric antimicrobial medication selection,(i.e., therapy selection in the absence of microbiology culture results),the disparities in disease severity and healthcare exposures between inpatients and primary care outpatients, surveillance data may not apply to both patient groups. As a result, using inpatient surveillance data to inform antibiotic prescribing in outpatient primary care seems doubtful. Clinicians may give second-line medicines unnecessarily if inpatient data overstated the degree of antimicrobial resistance detected in the outpatient context.[15]Therefore, the present study was planned to observe the local resistance patterns by formulating an annual cumulative antibiogram of in-patients along with an additional sub-analysis of the of the influence of age, gender, and location of bacterial isolates susceptibility.

So, to support the antimicrobial stewardship, we aimed

✓ To observe the antimicrobial susceptibilities of bacterial isolates from inpatients by constructing a local cumulative antibiogram for the year 2020 from January 1, 2020, to December 31, 2020.

✓ To observe the prevalence of ESKAPE pathogens among hospitalized patients.

✓ To observe the influence of age, gender, and location of bacterial isolates susceptibility.

MATERIALS AND METHODS:

Ethical Consideration:

This study was approved by Institutional Human Ethics Committee, Number: IHEC/721/2021 dated 04th August 2021, and permitted by the Member Secretary, Institutional Human Ethics Committee, Rajah Muthiah Medical College and Hospital, Annamalai University. The registration number of IEC is EC/NEW/INST/2020/1249.

Participants' informed consent was not required. No human participants were used in this investigation, and there was no consent process.

Study Site:

Rajah Muthiah Medical College and Hospital (RMMCH) is a tertiary care teaching hospital located in Chidambaram, Cuddalore district, Tamil Nadu, India. It has a bed strength of 1400 with modern A/C Operation Theatres. The hospital treats approximately 2800 to 3000 outpatients and around 1000 inpatients per day.

Study Design:

This is a retrospective cross-sectional study aimed at formulating a hospital-wide annual antibiogram for in-patients.

Study Duration:

The study required gathering data from the medical records of the inpatients satisfying the inclusion and exclusion criteria for the year 2020 from January 1, 2020, to December 31, 2020.

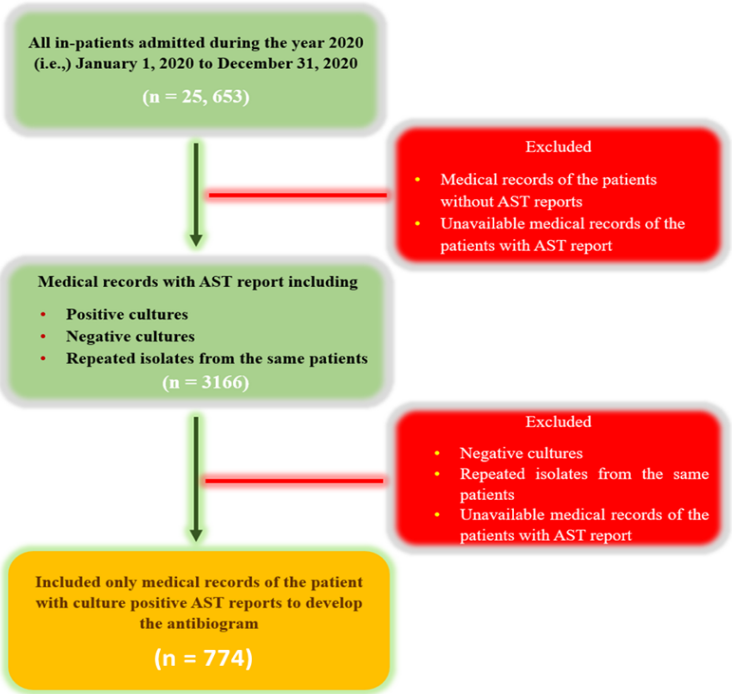


Figure No. 1: **STROBE diagram depicting the flow of the study population**

AST report – Antibiotic Susceptibility/Sensitivity report

Study Population:

All the inpatients from all the departments of the hospitals who were admitted during the year 2020 (January 1, 2020, to December 31, 2020) and subjected to Antimicrobial Susceptibility tests. The selection of patients for this study was based on the following inclusion and exclusion criteria (Figure 1).

Inclusion Criteria:

- The medical records of the in-patients with Microbiology Culture and Sensitivity report of all ages who were admitted during the year 2020 (January 1, 2020, to December 31, 2020).
- Only the first isolate of a given species per patient per analysis period regardless of body site or susceptibility profile for constructing the antibiogram.

Exclusion Criteria:

- Duplicate isolates of the same patient.
- Organisms with <10 isolates per analysis period
- Surveillance cultures.
- Isolates with intermediate or moderate susceptibilities.
- Medical records of in-patients from Intensive Care Units.
- Microbiology Culture and Sensitivity reports of laboratories other than the microbiology department of the hospital.
- Microbiology and culture sensitivity reports of outpatients during the year 2020 (January 1, 2020, to December 31, 2020).

Sample Size Determination:

A sample size of 384 patients was estimated by using a 95% confidence level, and 5% absolute precision using the formula a for a single proportion[16] where the proportion of patients with susceptibility to particular bacterial isolates is taken to be 50% and patients without susceptibility to particular bacterial isolates are 50%.

$$Sample\ size(n) = \frac{\left(Z_{1-\alpha/2}\right)^2 \times (p) \times (q)}{(d^2)}$$

$Z_{1-\alpha/2}$ = 95 % = 1.96

p = 50 %

q = 50 %

d = 5 %

Antimicrobial Susceptibility Testing:

The microbiology lab of the hospital receives different types of clinical specimens from both inpatients and outpatients. The specimens would then be cultured on appropriate culturing media according to national standard operating procedures and Clinical and Laboratory Standards Institutes (CLSI) guidelines. Furthermore, antibiotic susceptibility testing (AST) on the isolated/identified organism is done by applying the Kirby-Bauer disc diffusion method by producing the bacterial suspension and inoculating on Mueller-Hinton agar or Blood supplemented Mueller-Hinton agar. The following antibiotics were used: Amikacin (AK; 30 mcg), Amoxicillin/Clavulanic acid (AMC; 30 mcg), Ampicillin (AMP; 10 mcg), Cefoperazone (CPZ; 75 mcg), Cefotaxime (CTX; 10/30 mcg), Ceftazidime (CAZ; 30 mcg), Ceftriaxone (CTR; 30 mcg), Cefuroxime (CXM; 30 mcg), Chloramphenicol (C; 30 mcg), Ciprofloxacin (CIP; 5 mcg), Clindamycin(CD; 2 mcg), Erythromycin (E; 15 mcg), Gentamicin (GEN; 10 mcg), Imipenem (I; 10 mcg), Linezolid (LZ; 30 mcg), Meropenem (MEM; 10 mcg), Nitrofurantoin (NIT; 300 mcg), Norfloxacin (NX; 10 mcg), Oxacillin (OX; 5 mcg), Piperacillin/Tazobactam (PIT; 100/10 mcg), Tetracycline (TE; 30 mcg), Tobramycin (TOB; 10 mcg), Trimethoprim/Sulfamethoxazole (COT; 1.25/3.75 mcg).

Study Procedure:

- A standardized Data Abstraction Form was created to record the data necessary for developing the antibiogram.
- A simple random sampling technique was performed and each medical record of the patients was given a random number to maintain confidentiality.
- In addition to the data abstraction form, an abstraction procedural manual consisting of a clear and detailed explanation of the protocols and steps for data extraction was created to further ensure the reliability, accuracy, and consistency between us.

Sources of Data:

The following documents were referred from the medical records of the patients:

- Admission record
- Microbiology Culture & Sensitivity report

Data Collection:

The data abstraction form was divided into 4 sections as follows:

- Patient's demographics
- Hospital Admission
- Medical history and Diagnosis
- Results of the Microbiology Culture & Sensitivity tests

Statistical Analysis:

- The data entry was performed using Microsoft Excel 2016 and coded into two different statistical software for analysis.
- The frequency tables and descriptive statistics were used to describe the variables of interest.
- A cumulative Antibiogram was created using the software WHONET 2020[17] (Version 20.17.26) and Statistical analysis was done using IBM SPSS[18] Statistics software (Version 23). The WHO Collaborating Centre for Antimicrobial Resistance Surveillance at Brigham and Women's Hospital in Boston, Massachusetts, created and supports WHONET, a Windows-based database software program for the management and analysis of microbiology laboratory data with a specific focus on antimicrobial resistance surveillance.[17]
- The influence of age, gender, and location of bacterial isolates susceptibility were done using Chi-square, and a p-value of < 0.05 was considered significant.

RESULTS AND DISCUSSION:

The Indian populace is acknowledged to be the world's largest consumer of antibiotics. The antibiotic resistance situation in India has raised major public health concerns, prompting the

development of a control plan.[19] Our country is gradually becoming more aware of the threat of AMR. As a result, many regulatory organizations are implementing a variety of steps to combat this threat. The first major step in this direction was the first-ever meeting of medical societies in the country on the AMR issue, which brought together all stakeholders, including medical societies, various government bodies, media, academics, and international representatives, under one roof to discuss the issue. They developed actionable recommendations for dealing with AMR, which led to the production of the "Chennai Declaration," a declaration intended to raise overall awareness about AMR. Following this, the Antimicrobial Resistance Surveillance and Research Network (AMRSN) was founded by the Indian Council of Medical Research (ICMR) in 2013 to collect statewide evidence on AMR and make decisions based on it. In 2016, the first "National Antimicrobial Treatment Guidelines" document was published. These guidelines have aided many institutions in making more informed antibiotic decisions and enabling more effective antimicrobial stewardship programs. Except for a few tertiary care institutions, most Indian hospitals lack institutional antibiograms and policies to govern antimicrobial selection. As a result, greater antimicrobial coverage is now being used.[20]Therefore, the present study was conducted to observe the local resistance patterns by formulating an annual cumulative antibiogram of in-patients along with an additional sub-analysis of the influence of age, gender, and location of bacterial isolates susceptibility to support antimicrobial stewardship.

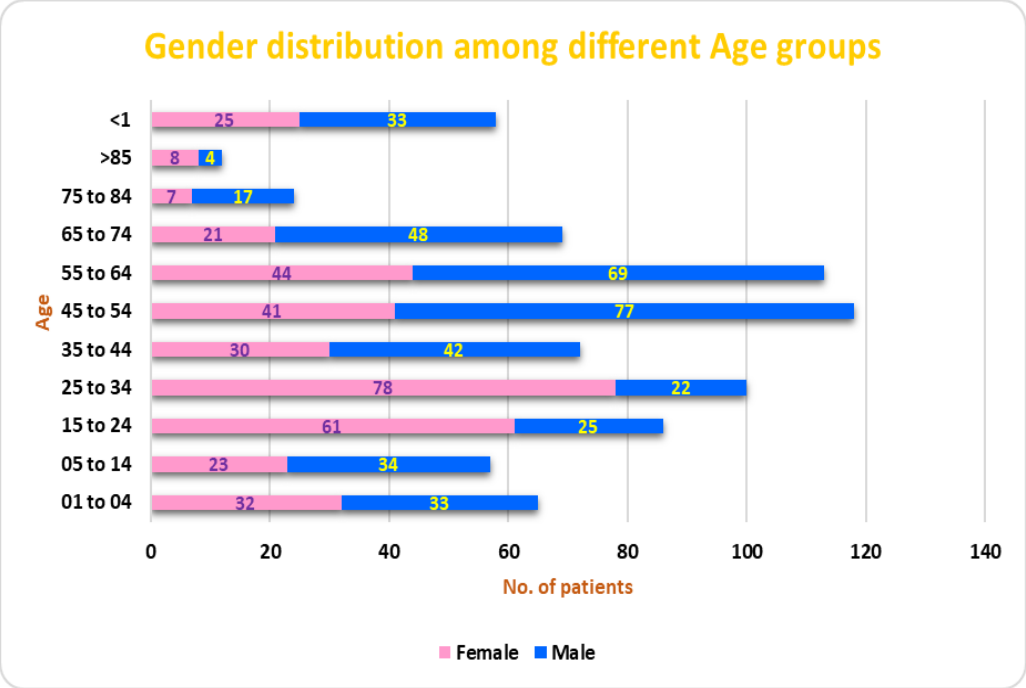


Figure No. 2: Demographics of patients

In the present study, a total of 774 medical records of the inpatients from different clinical departments of the hospitals with culture-positive Microbiology Culture & Sensitivity reports were included to develop the antibiogram.

Demographic data revealed that out of 774 patients, 404 (52.2 %) were males and 370 (47.8 %) were females. Qadeer *et al*,[21] conducted a similar study where 56.6 % males and 43.3 % were female patients. The majority of the patients were under the age category of 45 to 54, 118 (15.2 %). A higher male preponderance was observed under the age category of 45 to 54, 77 (9.9 %), and a higher female preponderance under the age category of 25 to 34, 78 (10.1 %). Figure 2 shows the distribution of gender among different age groups.

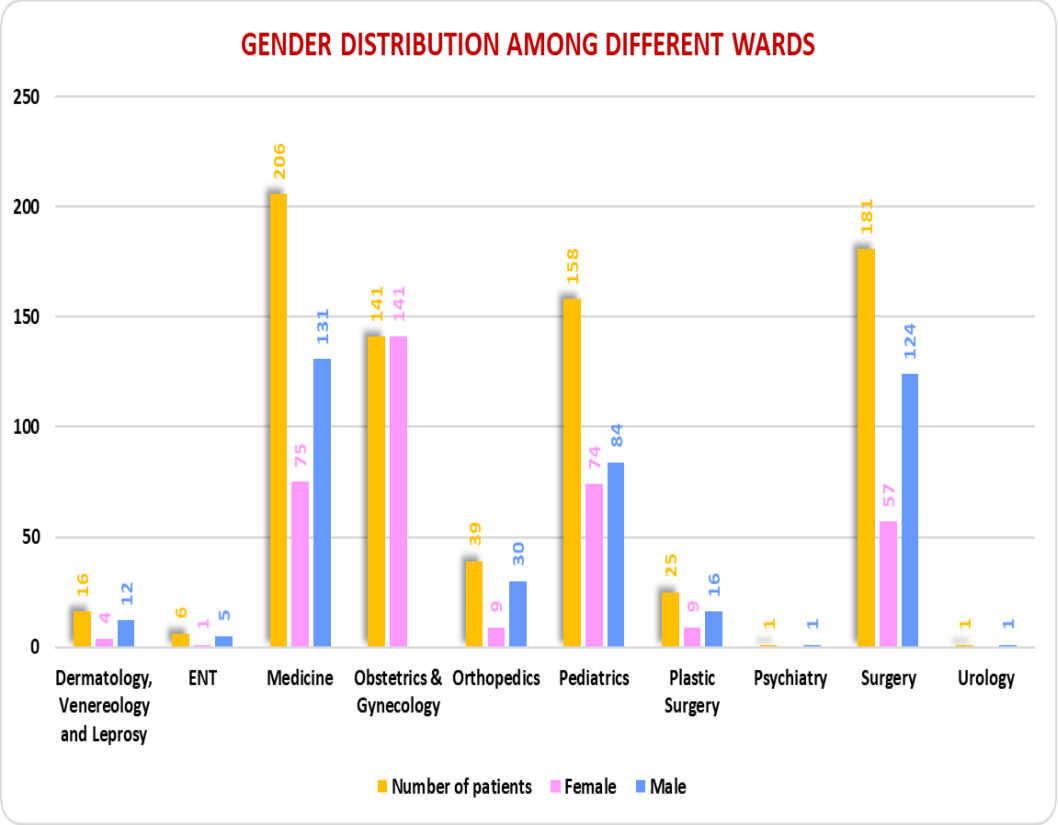


Figure No. 3: Distribution of Gender among different Wards

Figure 3 illustrates the Ward-wise distribution of gender. The medicine ward holds the highest number of patients 206 (26.6 %) with Culture & Sensitivity tests done followed by Surgery, 181 (23.4 %,) and Pediatrics, 158 (20.4 %) wards. The majority of the females are from Obstetrics & Gynecology ward, 141 (18.2 %) followed by Medicine, 75 (9.7 %), and Pediatric, 74 (9.5 %) wards. The majority of the males are from the Medicine ward, 131 (16.9

%) followed by Surgery, 124 (16.0 %), and Pediatrics, 84 (10.9 %) wards. The comparisons were statistically significant by the Chi-square test ($p < 0.001$).

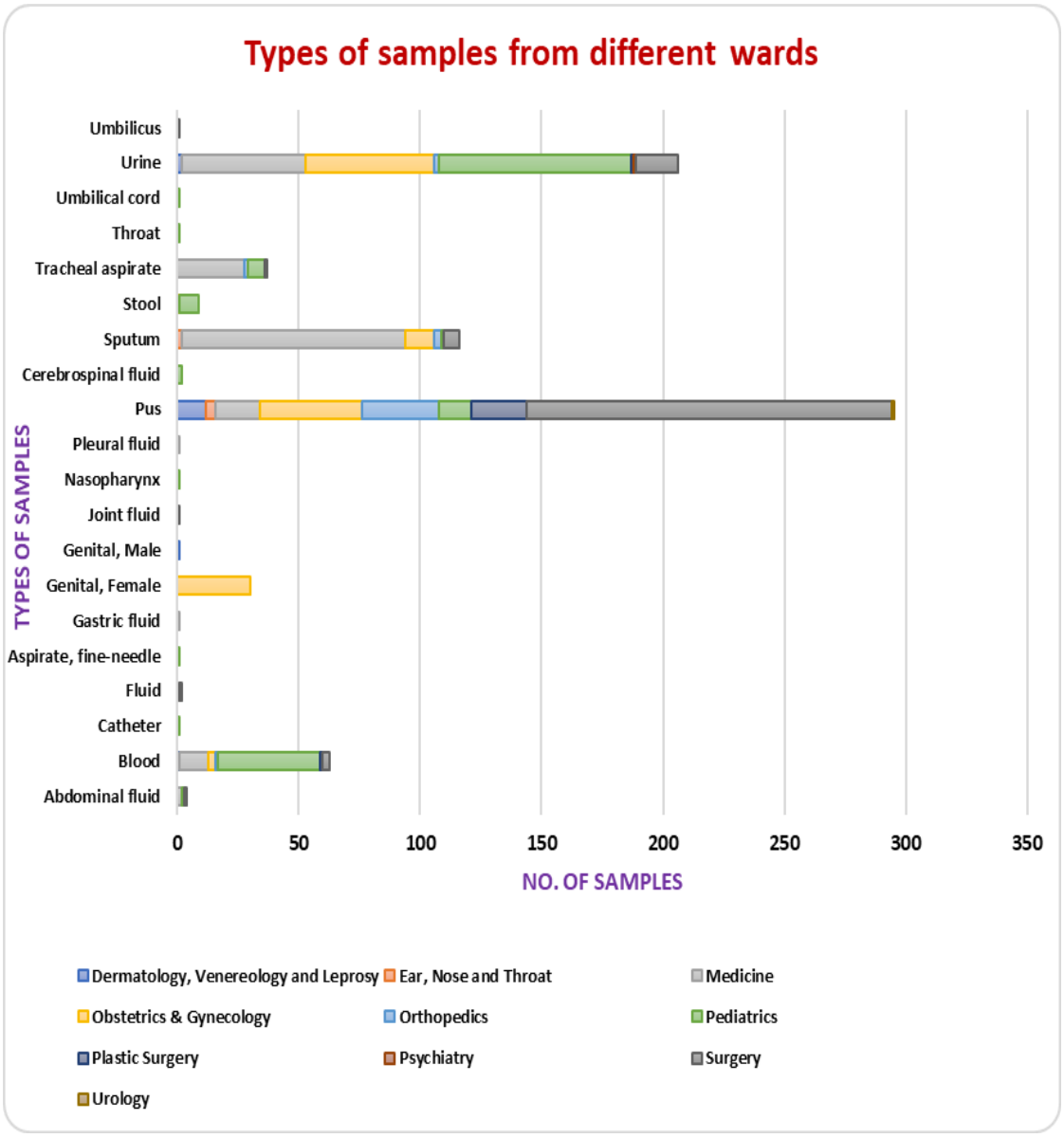


Figure No. 4: Types of samples from different Wards

Figure 4 illustrates the types of samples from different wards. Out of 774 isolates, Pus cultures were the highest, 295 (38.1 %) followed by Urine cultures, 206 (26.6 %), Sputum cultures, 116 (14.9 %), Blood cultures, 63 (8.1 %), Tracheal aspirates 37 (4.8 %) and Genital cultures, female 30 (4.0 %) which is in line with the study conducted by Divyashanthi *et al*.[22] Pus cultures were the highest in the surgery ward, 150 (19.3%) which is in accordance with a study conducted by Nureen*et al*,[23] which was particularly done to identify bacterial isolates in pus samples collected from patients in various hospital wards. Urine cultures were

the highest in the pediatric ward, 79 (10.2%). Sputum cultures were the highest in the medicine ward, 92 (11.9%). Blood cultures were the highest in the pediatric ward, 42 (5.4%). A higher number of tracheal aspirates were from the medical ward, 28 (3.6%) and a higher number of genital cultures of females were from the obstetrics and Gynecology ward, 30 (3.9 %) The comparisons were statistically significant by the chi-square test ($p < 0.001$).

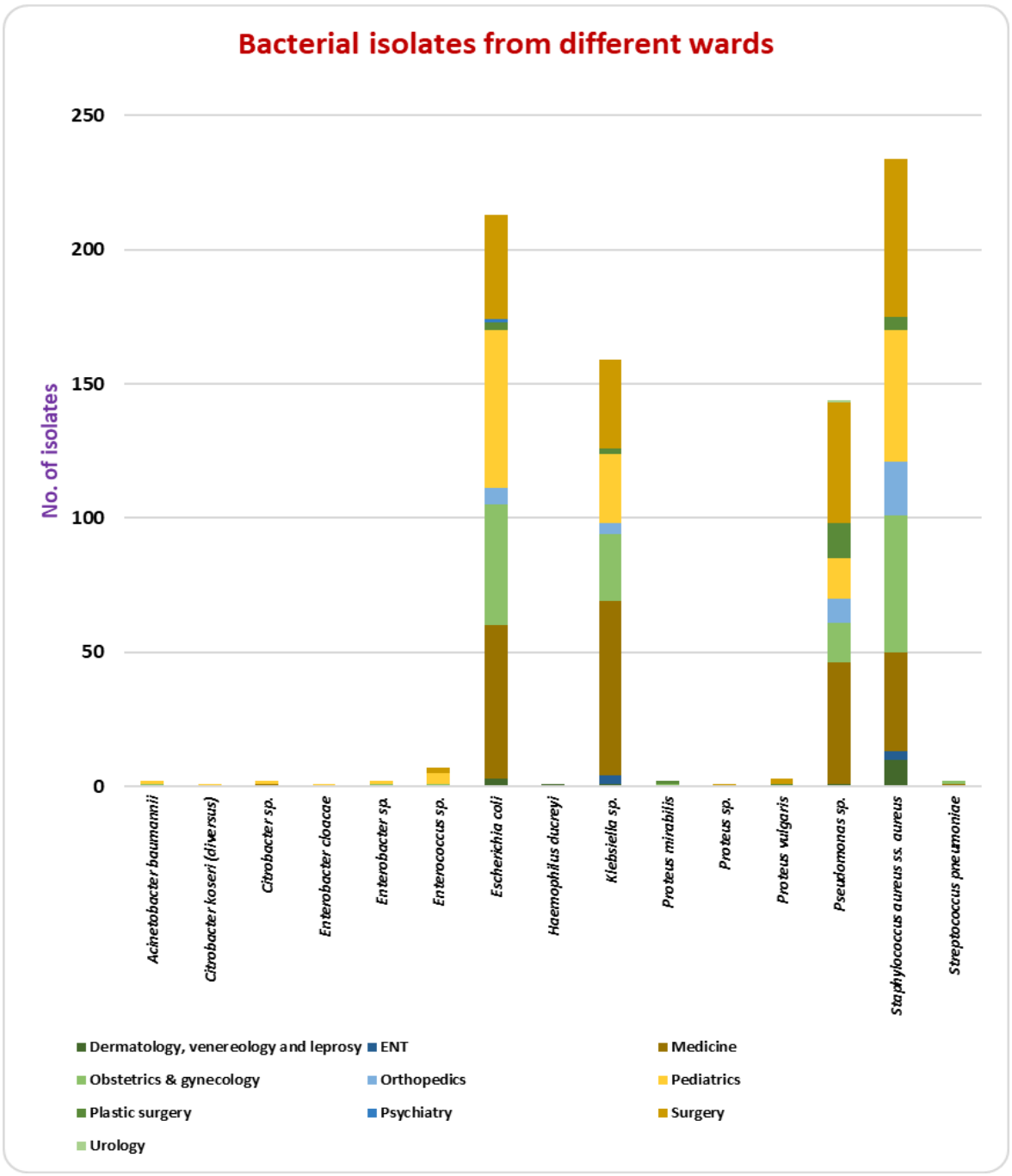
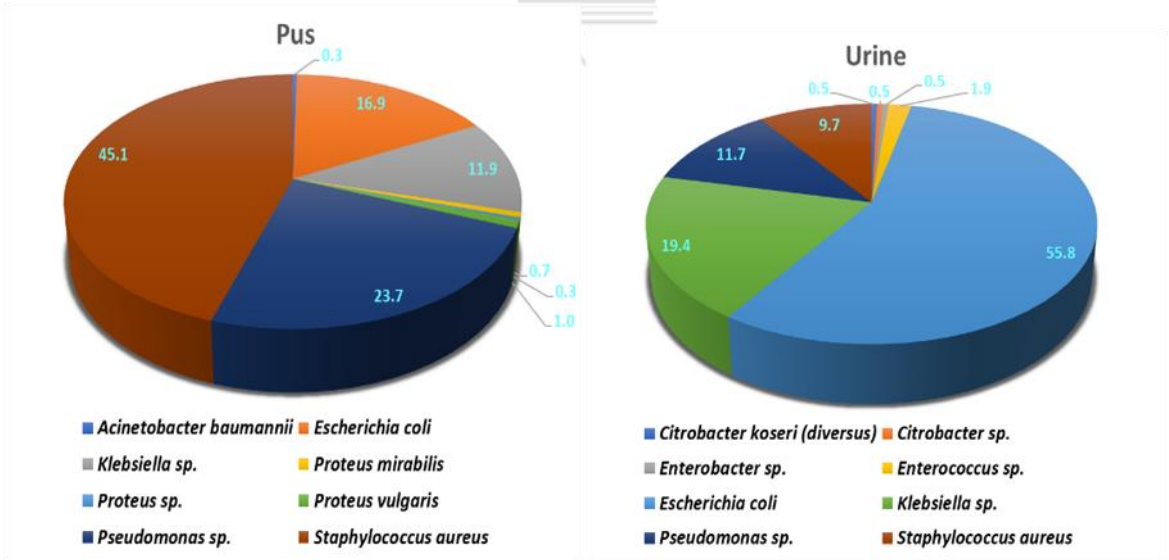


Figure No. 5: Bacterial Isolates from different Wards

Figure 5 displays the percentage of bacterial isolates from different wards. The most predominant organism was *Staphylococcus aureus*, 234 (30.2 %), followed by *Escherichia coli*, 213 (27.5 %), *Klebsiella sp*., 159 (20.5 %), and *Pseudomonas sp*., 144 (18.6 %). *Staphylococcus aureus* was the most prevalent in the surgery ward which is consistent with a study conducted by Misha *et al*, 59 (7.6 %). *Escherichia coli* was the most prevalent in the pediatric ward, 59 (7.6 %). *Klebsiella sp*. was the most prevalent in the medicine ward, 65 (8.4 %), and *Pseudomonas sp*. was the most prevalent in the medicine and surgery wards of the hospital, 45 (5.8 %). The comparisons were statistically significant by the Chi-square test ($p < 0.001$).

The Indian Council for Medical Research (ICMR) initiated antimicrobial resistance surveillance and research in 2013. It now contains sixteen regional centers and six nodal centers. Regional facilities around the country will track antimicrobial profile trends.

The % distribution of bacterial isolates from predominant samples is presented in Figure 6. Out of 774 samples, Pus cultures were the highest, 295 (38.1 %) followed by Urine cultures, 206 (26.6 %), Sputum cultures, 116 (14.9 %), Blood cultures, 63 (8.1 %), Tracheal aspirates 37 (4.8 %) and Genital cultures, female 30 (4.0 %).



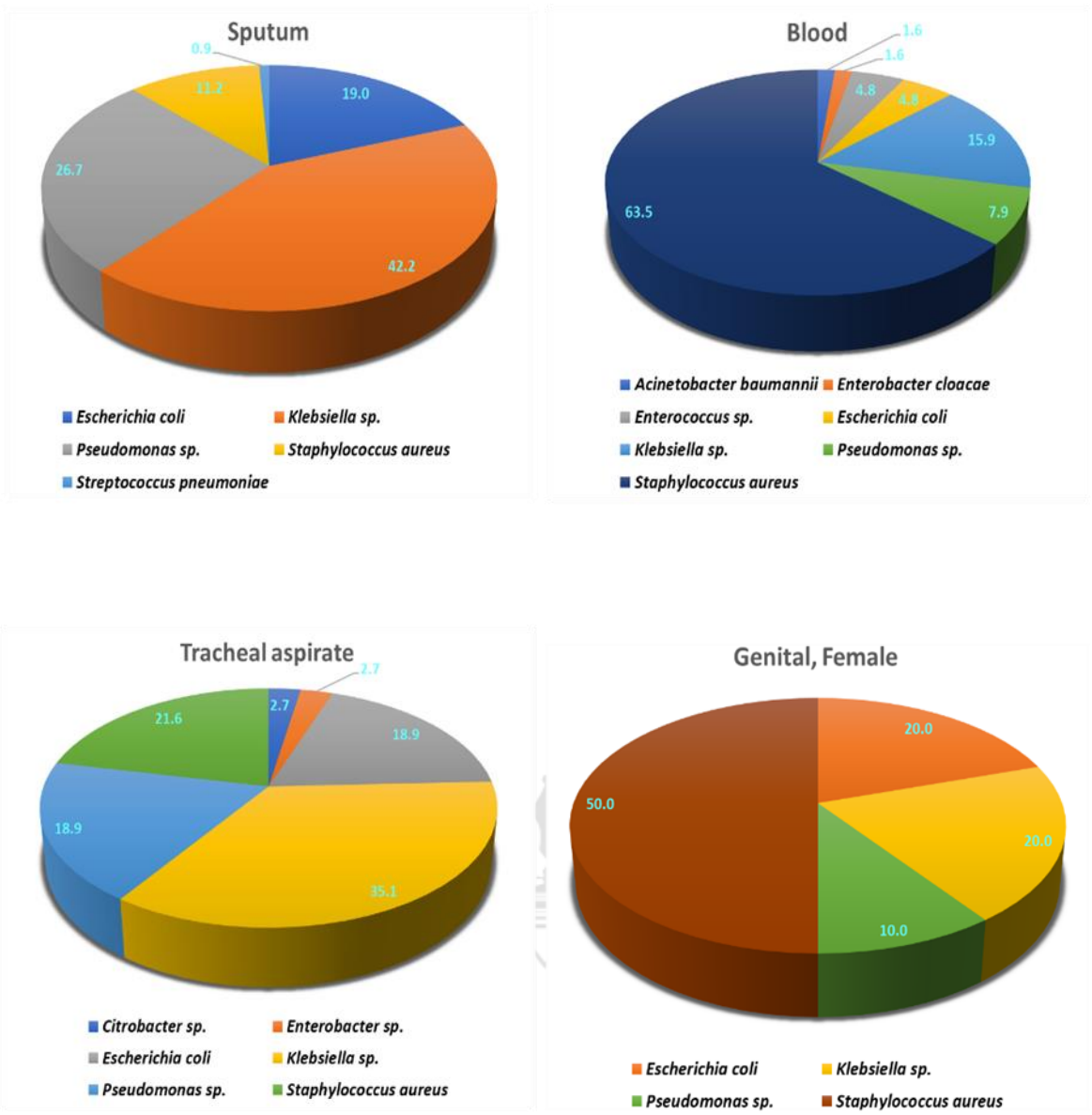


Figure No. 6: % Distribution of bacterial isolates from predominant samples

Out of 295 pus samples, the most frequently isolated species were *Staphylococcus aureus*, 133 (45.1 %) followed by *Pseudomonas spp.*, 70 (23.7 %), *Escherichia coli*, 50 (16.9 %), and *Klebsiella spp.*, 35 (11.9 %). Out of 206 urine samples, the most frequently isolated species were *escherichia coli*, 115 (55.8 %) followed by *Klebsiella spp.*, 40 (19.4 %), *Pseudomonas spp.*, 24 (11.7 %), and *Staphylococcus aureus*, 20 (9.7 %). Out of 116 sputum samples, the most frequently isolated species were *Klebsiella spp.*, 49 (42.2 %), *Pseudomonas spp.*, 31 (26.7 %), *Escherichia coli*, 22 (19.0 %), and *Staphylococcus aureus*, 13 (11.2 %). Out of 63 blood samples, the most frequently isolated species were *Staphylococcus aureus*, 40 (63.5 %), *Klebsiella spp.*, 10 (15.9 %), and *Pseudomonas spp.*, 5 (7.9 5). Out of 37 tracheal aspirates, the most frequently isolated species were *Klebsiella spp.*, 13 (35.1 %),

Staphylococcus aureus, 8 (21.6 %), *Escherichia coli*, 7 (18.9 %), and *Pseudomonas spp.*, 7 (18.9 %). Out of 30 genital samples (female), the most frequently isolated species were *Staphylococcus aureus*, 15 (50.0 %) followed by *Escherichia coli*, 6 (20 %), *Klebsiella spp.*, 6 (20 %), and *Pseudomonas spp.*, 3 (10 %). These findings were consistent according to Indian Council for Medical Research's (ICMR)Antimicrobial Resistance Research & Surveillance Network (AMRSN) annual report of 2020, in which, *Staphylococcus aureus* was the most prevalent in the pus specimens; *Escherichia coli* was found to be the predominant bacteria in the urine specimens and *Klebsiella spp.*, in the sputum samples and tracheal aspirates. *Klebsiella spp.* was high in the blood specimen which is contrary to our findings where Staphylococcus aureus was higher in the blood specimens in the present study.[24]Antimicrobial resistance is exacerbated by the frequency of ESKAPE pathogens. Because they are commonly resistant to (escape the effects of) currently available antimicrobial therapies, they are the most dangerous bacterial infections in hospitals., resulting in hospital-acquired infections.[6]Surgical site infections are common postoperative consequences, accounting for 14 percent to 16 percent of all hospital-acquired infections. ESKAPE bacteria linked to surgical site infections have substantial resistance rates.[25] According to a recent study, the discovery of significant acquired resistance among hospitalized patients and the frequent isolation of ESKAPE bacteria raises concerns and shows that these organisms have disseminated across the community. Understanding the epidemiology of bacterial infections in a given area can help with the development of local empirical treatment procedures.[26]

Table 1 depicts that the prevalence of ESKAPE pathogens among the bacterial isolates was (n = 549) 70.9 %. The most predominant were the ***Staphylococcus aureus*** (n = 234) 30.2 % followed by ***Klebsiella spp.,*** (n = 159) 20.5 %, ***Pseudomonas aeruginosa*** (n = 144) 18.6 % and ***Enterococcus spp.,*** (n = 7) 0.9 %. All these pathogens were higher among male patients compared to females except *Enterobacter spp.,* Methicillin–Susceptible *Staphylococcus aureus*, and *Enterococcus spp*. These findings exactly match the study conducted by Benko *et* [26]that looked into the epidemiology and resistance trends of bacterial isolates from a tertiary-care Emergency Department over five years, with an emphasis on ESKAPE bacteria (including the Enterobacterales group).

Table No. 1: The distribution of ESKAPE isolates among Male and Female patients

GENUS	SPECIES		NUMBER	MALE	FEMALE
Enterobacter	*Enterobacter spp.*		**2**	**0**	**2**
	Enterobacter cloacae		**1**	**1**	**0**
Staphylococcus	*S. aureus*	MRSA	**229**	**115**	**114**
		MSSA	**5**	**2**	**3**
Klebsiella	*Klebsiella spp.*		**159**	**82**	**77**
Acinetobacter	*A. baumannii*		**2**	**1**	**1**
Pseudomonas	*P. aeruginosa*		**144**	**94**	**50**
Enterococci	*Enterococcus spp.*		**7**	**2**	**5**

The data from cumulative antibiogram reports is crucial in determining which empirical antibacterial medication to use. Antibiogram is a multipurpose record that, in addition to displaying the institution's antibiotic susceptibility pattern, provides a vivid depiction of the species that cause sickness the most in various hospital units.[27] These days, nosocomial infections are a serious public health problem and a leading cause of mortality and morbidity among hospitalized patients. They impact 7 to12 percent of hospitalized patients globally, with approximately 1.4 million people suffering from infections contracted in hospitals.[28]The current study focuses solely on bacterial isolate susceptibility rates among in-patients.

The Clinical Laboratory Standards Institute (CLSI, formerly NCCLS) is a non-profit organization that promotes the development and adoption of voluntary consensus standards and guidelines in the healthcare field. To assist health care facilities, the organization issued "Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data: Approved Guideline" (NCCLS M39-A). The in-patient antibiogram which was created following the revised NCCLS M39-A Antibiogram Recommendations is shown in Figure 7.

✓ Only the first isolate of a given species per patient per analysis period was included regardless of body site or susceptibility profile; duplicate isolates from the same patient were excluded.

✓ Separate tables have been used for Gram-positive and Gram-negative bacteria.

✓ Only organisms with ≥ 10 isolates per analysis period were included.

✓ Surveillance cultures were excluded.

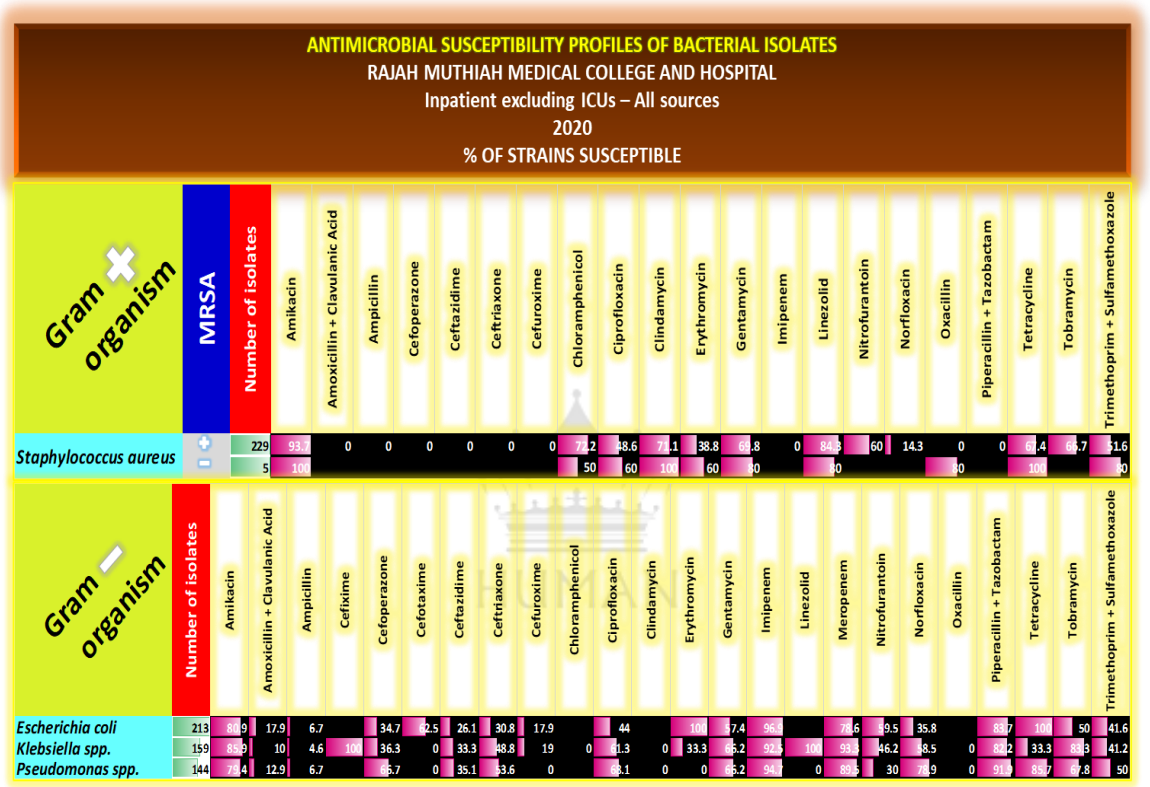


Figure No. 7: In-Patient Antibiogram for the year 2020

In the present study, amongst the gram-positive isolates, *Staphylococcus aureus* was the most prevalent species (n = 235), of which 229 were Methicillin-Resistant *Staphylococcus aureus* (30.4 %), and 5 were found to be Methicillin–Sensitive *Staphylococcus aureus* (0.6 %). The most prevalent cause of SSIs (Surgical Site Infections) is *Staphylococcus aureus*, which accounts for up to 37% of SSI cases in community hospitals, with MRSA being of special concern. According to the CDC, the percentage of SSIs caused by *Staphylococcus aureus* surged from 16.6% to 30.9 % between 1992 and 2002, while the number of methicillin-resistant S. aureus (MRSA) isolates increased from 9.2% to 49.3%. MRSA is becoming more common over the world, with significant regional diversity. Furthermore, tracking of

surveillance data has revealed that methicillin-resistant *Staphylococcus aureus* (MSSA) tends to grow into MRSA in hospital settings, a common cause of postoperative infection. In our investigation, Methicillin-resistant *Staphylococcus aureus* was the most common organism found in the surgical ward, indicating an increased risk of surgical-site infections. Pal *et al*,[29] revealed in a recent study to present an overview of the existing epidemiological data on the incidence of SSIs caused by *S. aureus* in a tertiary care center/health care setting that 269 (20.8 percent) of 1294 patients had SSIs. A total of 269 samples were tested, with 258 (95.9%) yielding bacterial growth and 267 bacterial isolates recovered. *Staphylococcus aureus* was the most prevalent organism (45.3 %).

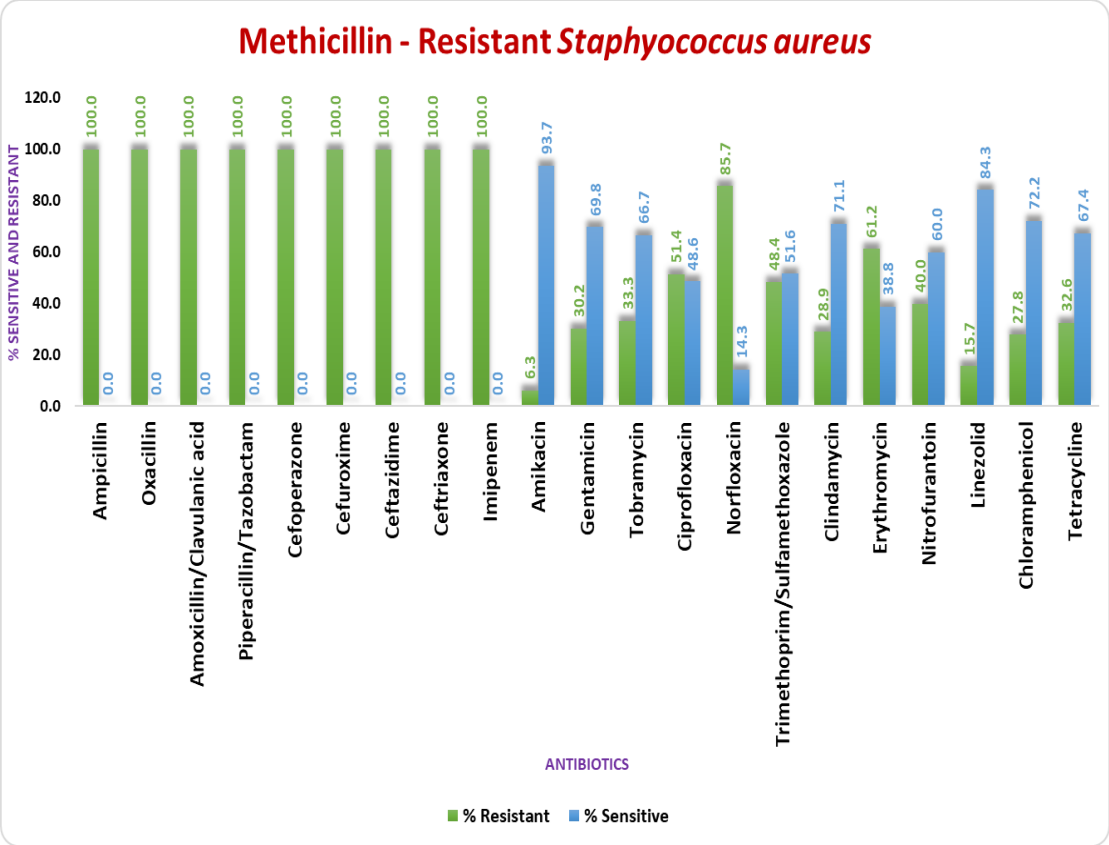


Figure No. 8: Antibiotic susceptibility profile of Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Figure 6 illustrates the antibiotic susceptibility profile of Methicillin-resistant s*taphylococcus aureus* (MRSA). Higher resistance rates were observed with Ampicillin (100 %), Oxacillin (100 %), Amoxicillin/Clavulanic acid (100 %), Piperacillin/Tazobactam (100 %), Cefoperazone (100 %), Cefuroxime (100 %), Ceftazidime (100 %), Ceftriaxone (100 %), Imipenem (100 %), Norfloxacin (85.7 %, Erythromycin (61.2 %), and Ciprofloxacin (51.4

%). These findings were consistent with the study conducted by Vasuki *et al*,[30]where MRSA isolates from a tertiary care teaching hospital in South India were resistant to Penicillins, Beta-lactamase inhibitors, and Third-generation cephalosporins. In the present study, MRSA isolates are more prevalent in the surgery ward of the hospital. In addition to that, these classes of antibiotics were more commonly prescribed in the surgery ward of the hospital post-operatively and this may contribute to an increased incidence of postoperative surgical infections. Highest rate of susceptibility was seen towards Amikacin (93.7 %), Linezolid (84.3 %), Chloramphenicol (72.2 %), Clindamycin (71.1 %), Gentamycin (69.8 %), Tetracycline (67.4 %), Tobramycin (66.7 %), Nitrofurantoin (60.0 %) and Trimethoprim/Sulfamethoxazole (51.6 %).Similarly, the susceptible patterns of MRSA isolates were in accordance with the above study conducted by Vasuki *et al*,[30] where Amikacin and Linezolid were highly susceptible.

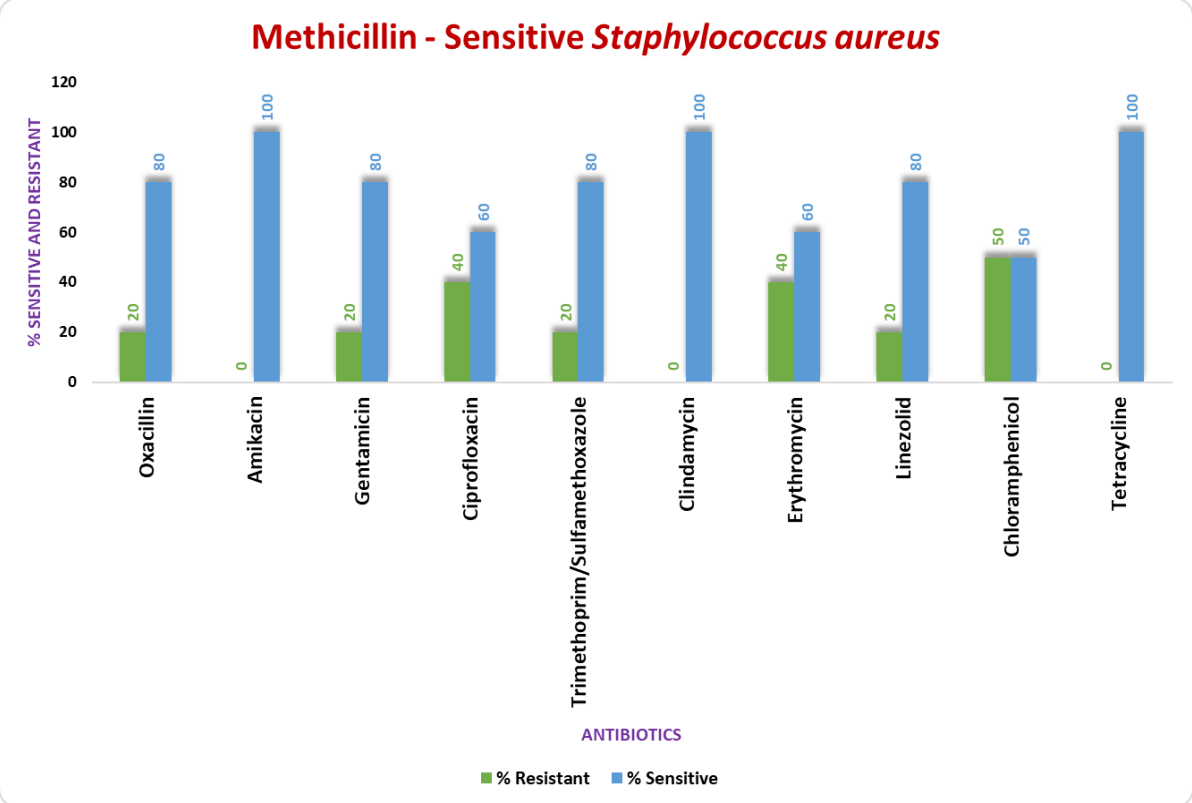


Figure No. 9: Antibiotic susceptibility profile of Methicillin–Sensitive *Staphylococcus aureus* (MSSA)

Figure 7 illustrates the antibiotic susceptibility profile of Methicillin–Sensitive *Staphylococcus aureus* (MSSA). Higher resistance rates were observed with Chloramphenicol (50 %), Erythromycin (40 %), and Ciprofloxacin (40 %). Preeja *et al*,[31]

found that Chloramphenicol was the least resistant antibiotic in their study (1 %). Whereas, the resistance of *Staphylococcus aureus* to fluoroquinolones is rising. According to Bouchiat C *et al*,[32]MSSA demonstrated 54.5 % resistance to Ciprofloxacin and 45.5 % resistance to Erythromycin in the study conducted in Bangalore. Highest rate of susceptibility was seen towards Amikacin (100 %), Clindamycin (100 %), Tetracycline (100 %), Oxacillin (80 %), Gentamycin (80 %), Trimethoprim/Sulfamethoxazole (80 %), Linezolid (80 %), Erythromycin (60 %) and Chloramphenicol (50 %). These findings were in line with a study conducted by Preeja *et al*,[31] where MSSA showed the least resistance or no resistance (0 %) to Amikacin. Multi-Drug Resistance among MSSA is a big source of concern, as it will spread throughout hospitals and into the community, complicating patient management. Infection management strategies have successfully reduced the frequency of invasive MRSA in healthcare settings. However, the burden of invasive *S. aureus* and death rates remain a source of worry. Continuous surveillance and antibiotic stewardship programs may aid in the prevention of MSSA transmission and the rise of MDR.

Amongst the gram-negative isolates, *Escherichia coli* (n = 213) was the most prevalent species followed by *Klebsiella spp.,* (n = 159) and *Pseudomonas spp.,* (n = 144).*Escherichia coli, Staphylococcus aureus, K. pneumoniae, S. pneumoniae, Acinetobacter baumannii,* and *Pseudomonas aeruginosa* were the bacteria responsible for more than 250 000 deaths related with AMR in 2019.[33]Between 2004 and 2007, *Escherichia coli* isolates from the community in India (n = 1,815) demonstrated increased resistance to ampicillin, nalidixic acid, and co-trimoxazole (75 %, 73 %, and 59 %, respectively). Injectables such as aminoglycosides are resistant to about a third of isolates (Gentamicin). The resistance of *Escherichia coli* to third-generation cephalosporins grew from 70% to 83 % between 2008 and 2013, whereas fluoroquinolones resistance climbed from 78 to 85 %. In 2008, ten percent of *E. coli* isolates were carbapenem-resistant, rising to thirteen percent in 2013.[34]

Figure 8 depicts the antibiotic susceptibility profile of *Escherichia coli.* Higher resistance rates were observed with Ampicillin (93.3 %), Amoxicillin/clavulanic acid (82.1 %), Cefuroxime (82.1 %), Ceftazidime (73.9 %), Ceftriaxone (69.2 %), Norfloxacin (64.2 %), Trimethoprim/Sulfamethoxazole (58.4 %), Ciprofloxacin (56.0 %) and Tobramycin (50.0 %). Selin Chiriyankandath Joy *et al*,[35] reported the least sensitivity of *E. coli* to Ampicillin in their study which is consistent with the present study.

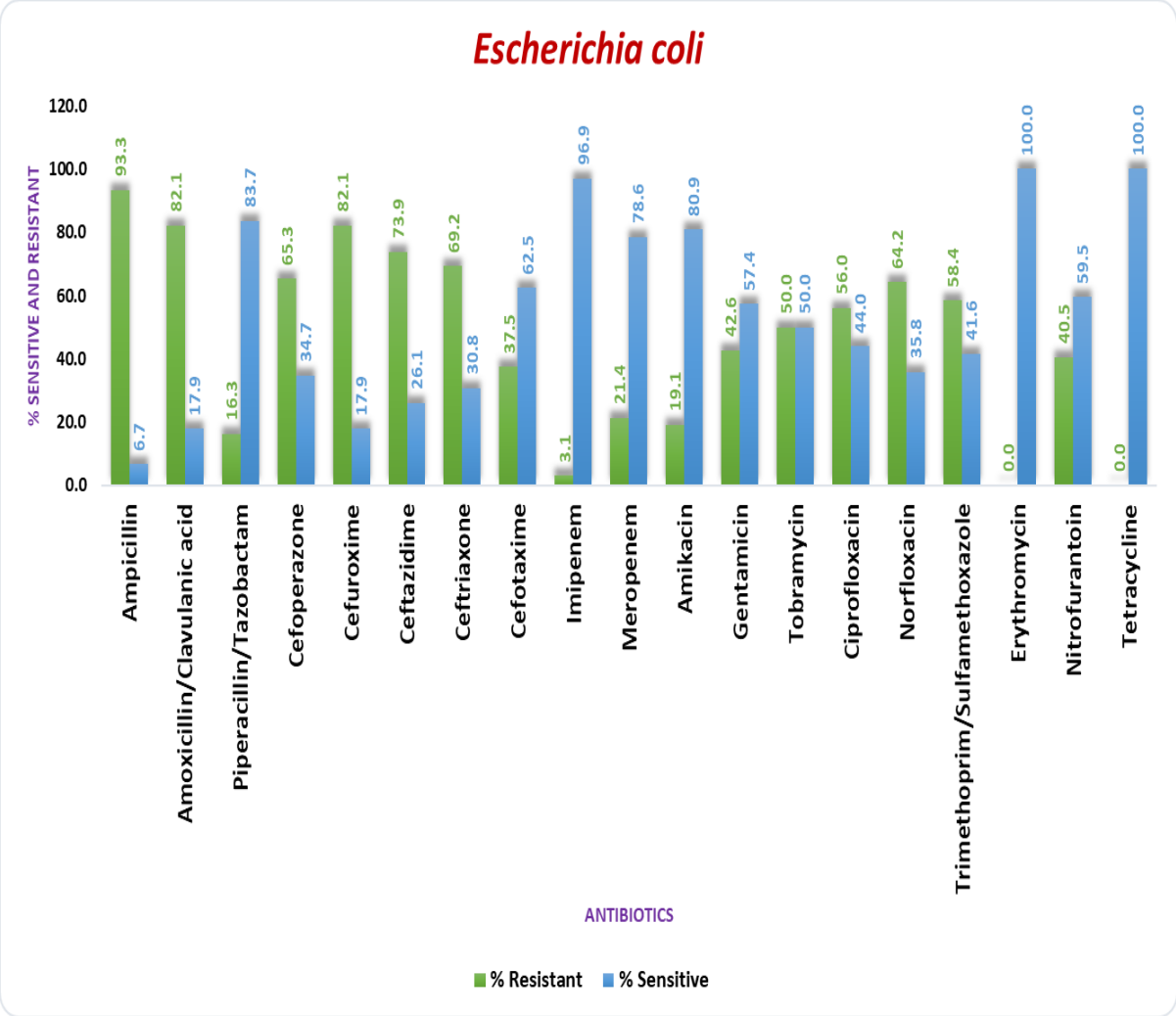


Figure No. 10: Antibiotic susceptibility profile of *Escherichia coli*

The highest rate of susceptibility was seen towards Erythromycin (100 %), Tetracycline (100 %), Imipenem (96.9 %), Piperacillin/Tazobactam (83.7 %), Amikacin (80.9 %), Meropenem (78.6 %), Cefotaxime (62.5 %), Nitrofurantoin (59.5 %), Gentamycin (57.4 %), and, Tobramycin (50.0 %). These findings were following the Indian Council for Medical Research's (ICMR) Antimicrobial Resistance Research & Surveillance Network (AMRSN) annual report of 2020where Urine isolates of *E. coli* were sensitive to Amikacin (84 %)and Imipenem (80 %).(24) Besides this, a study conducted by Yitayeh *et al*,[36]to evaluate the antimicrobial susceptibility patterns of community-acquired uropathogenic *E. coli* reported an increasing trend of susceptibility of E. coli towards Imipenem and Amikacin. The most AMR-related deaths in 2019 were caused by *Escherichia coli*, followed by *Klebsiella pneumoniae*, *Staphylococcus aureus, Acinetobacter baumannii*, *Streptococcus pneumoniae*, and *Mycobacterium tuberculosis*. Cephalosporin-resistant *E. coli* and fluoroquinolone-

resistant *E. coli* were two of the six pathogens – drugs that caused 50 000 to 100 000 deaths due to resistance in 2019.[33]

Figure 9 depicts the antibiotic susceptibility pattern of *Klebsiella spp.* Higher resistance rates were observed with Oxacillin (100 %), Cefotaxime (100 %), Clindamycin (100 %), Chloramphenicol (100 %), Ampicillin (95.4 %), Amoxicillin/clavulanic acid (90 %), Cefuroxime (81 %), Ceftazidime (66.7 %), Erythromycin (66.7 %), Tetracycline (66.7 %) and Cefoperazone (63.8 %). These findings were following a study conducted by Gashe *et* al,[37] which reported that microbial resistance to third-generation cephalosporin drugs has been increasing significantly.

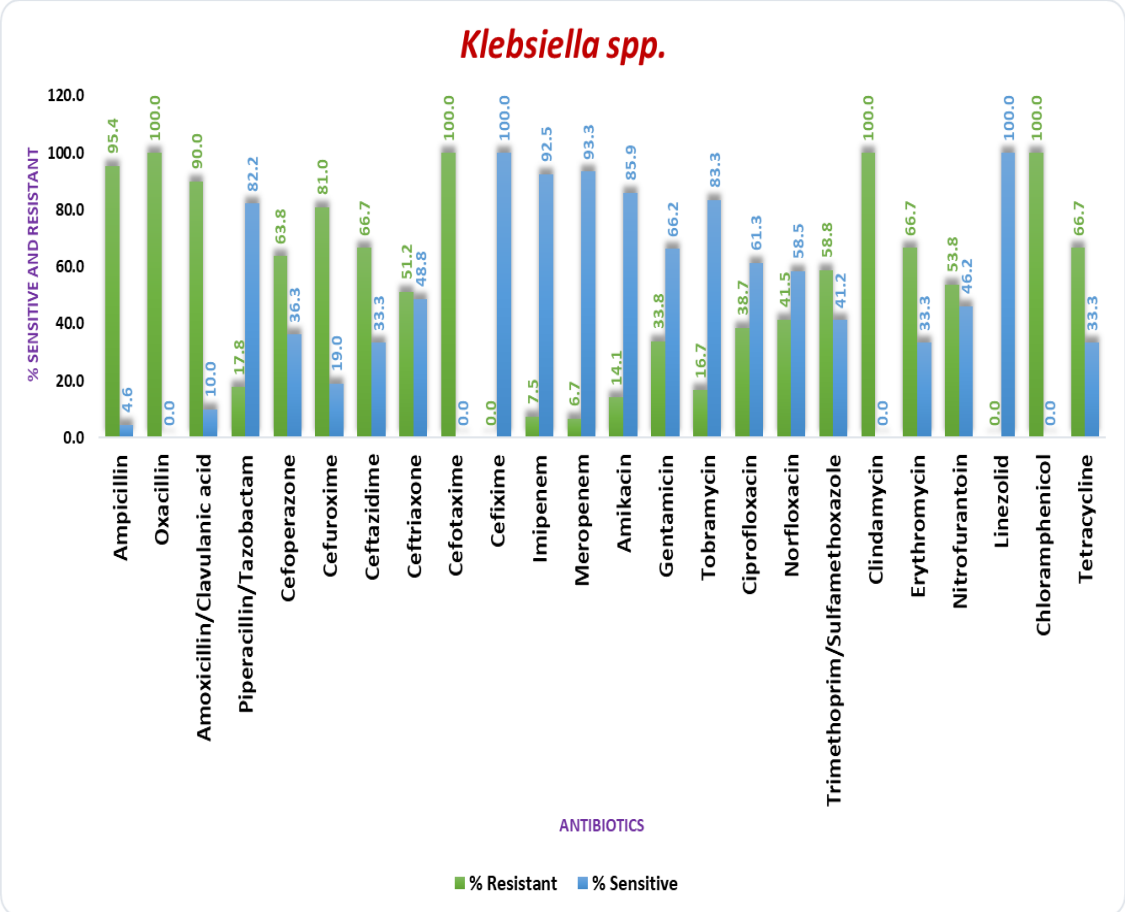


Figure No. 11: Antibiotic susceptibility pattern of *Klebsiella spp.*

In the present study, *Klebsiella spp.* was predominant in the medicine (8.5 %) and surgery wards (4.3 %) of the hospital and the most commonly prescribed antibiotics in these wards were Amoxicillin/ clavulanic acid, and Cefotaxime. In addition this, these findings were consistent with the study conducted by Gill M. K. *et al*,[38]which analyzed *Klebsiella pneumoniae* isolated from various clinical samples of hospitalized patients in a tertiary care

hospital in North India. Highest rate of susceptibility was seen towards Cefixime (100 %), Linezolid (100 %), Meropenem (93.3 %), Imipenem (92.5 %), Amikacin (85.9 %), Tobramycin (83.3 %), Piperacillin/Tazobactam (82.2 %), Gentamycin (66.2 %), Ciprofloxacin (61.3 %), and, Norfloxacin (58.5 %). Similar findings were reported in a study conducted by Gill M. K. *et al*.[38]

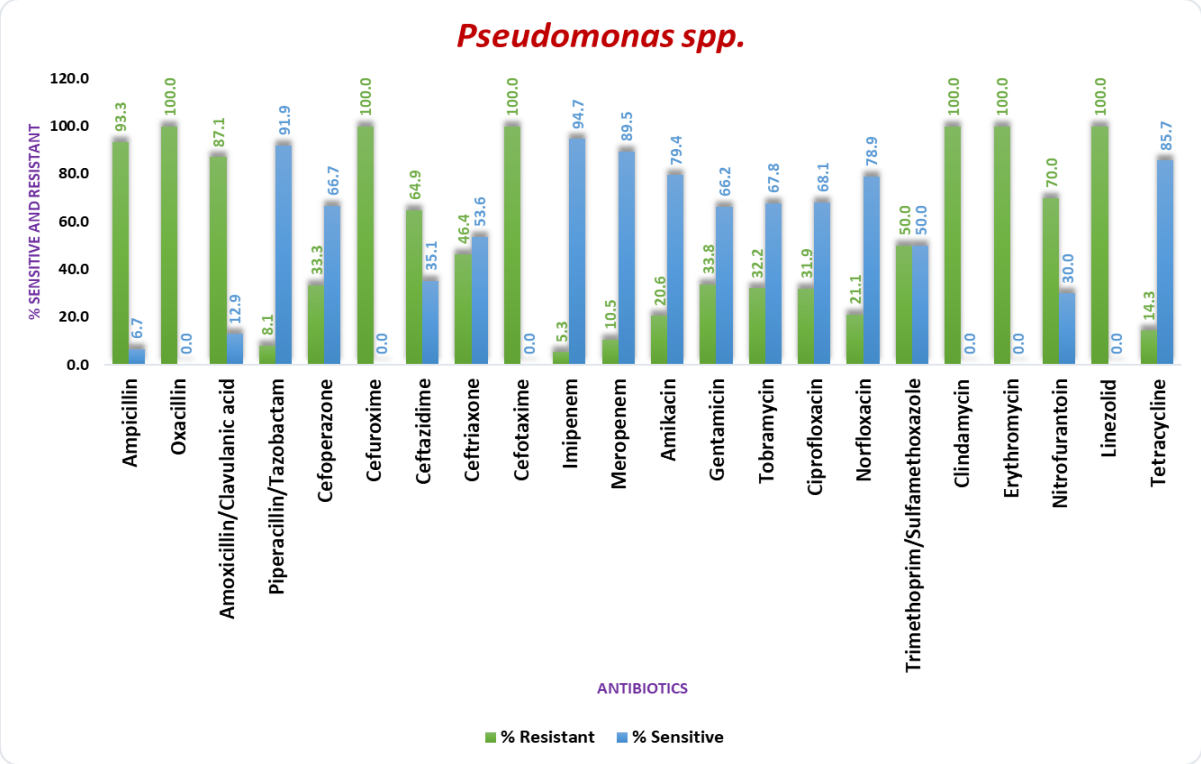


Figure No. 12 Antibiotic susceptibility pattern of *Pseudomonas spp.*

Figure 10 shows the antibiotic susceptibility pattern of *Pseudomonas spp.* Higher resistance rates were observed with Cefotaxime (100 %), Cefuroxime (100 %), Oxacillin (100 %), Clindamycin (100 %), Erythromycin (100 %), Linezolid (100 %), Ampicillin (93.3 %), Amoxicillin/clavulanic acid (87.1 %), Nitrofurantoin (70 %), Ceftazidime (64.9 %), and Trimethoprim/Sulfamethoxazole (50 %). In the present study, *Pseudomonas spp.* was more prevalent equally in the medicine and surgery wards of the hospital (5.8 %) and the number of prescriptions for Amoxycillin/Clavulanic acid, Cefotaxime as pre-operative antibiotics is high. Highest rate of susceptibility was seen towards Imipenem (94.7 %), Piperacillin/Tazobactam (91.9 %), Meropenem (89.5 %), Tetracycline (85.7 %), Amikacin (79.4 %), Ciprofloxacin (68.1 %), Tobramycin (67.8 %), Cefoperazone (66.7 %), Gentamycin (66.2 %), Ceftriaxone (53.6 %), and, Trimethoprim/Sulfamethoxazole (50 %).These findings were consistent with the study conducted by Rahman *et al*.[39]

The age and gender of patients affect the prevalence of bacterial infections. Bacterial resistance levels may also be affected by the patient's placement in the hospital. "Approximately 70% of patients admitted to a room previously occupied by a patient with *Clostridium difficile*, *Pseudomonas aeruginosa*, Methicillin-Resistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii*, or Vancomycin-Resistant *Enterococci* (VRE) are likely to contract these microbes during their hospital stay".[40]

Table No. 2: The resistance pattern of the most prevalent bacteria among the in-patients concerning age

Organisms	Adults (%) n	Pediatrics (%) n	Newborn (%) n	p-value	Antibiotics
S. aureus	**41. 6 (92/221)**	**4. 1 (9/221)**	**5.9 (13/221)**	**0.007**	**Ciprofloxacin**
E. coli	**68.4 (26/38)**	**13.1 (5/38)**	**0**	**0.021**	**Amoxicillin / Clavulanic Acid**
	41.2 (45/109)	**23 (25/109)**	**0**	**0.019**	**Norfloxacin**
Klebsiella spp.	**48 (62/129)**	**2.3 (3/129)**	**2.3 (3/129)**	**0.007**	**Ceftriaxone**
	14 (22/157)	**1.3 (2/157)**	**2.5 (4/157)**	**0.005**	**Piperacillin/ Tazobactam**
Pseudomonas spp.	**30 (6/20)**	**40 (8/20)**	**0**	**0.017**	**Nitrofurantoin**
	28.3(34/120)	**3.3 (4/120)**	**0.8 (1/120)**	**0.007**	**Tobramycin**

Out of 774 bacterial isolates from various specimens included in this study, 608 (78.5 %) were exposed to Ciprofloxacin, 198 (25.6 %) were exposed to Amoxicillin/Clavulanic Acid, 218 (28.2 %) were exposed to Ampicillin, 773 (99.8 %) were exposed to Amikacin, 342 (44.2 %) were exposed to Ceftriaxone, 187 (24.2 %) were exposed to Norfloxacin, 189 (24.4 %) were exposed to Nitrofurantoin, 148 (19.1 %) were exposed to Tobramycin, 531 (68.6 %) were exposed to Piperacillin/ Tazobactam and 615 (79.5 %) were exposed to Trimethoprim/Sulfamethoxazole. Exposure of antibiotics to micro-organisms is unevenly distributed.

Table 2 describes the resistance pattern of the most prevalent bacteria among the in-patients concerning age. It was observed that the resistance for the organisms ***Staphylococcus aureus*** to Ciprofloxacin (41.6 %, p = 0.007), ***Escherichia coli*** to Amoxycillin/ Clavulanic Acid (68.4 %, p = 0.021) and Norfloxacin (41.2 %, p = 0.019), ***Klebsiella spp***. to Ceftriaxone (48 %, p = 0.007) and Piperacillin/Tazobactam (14 %, p = 0.005) and ***Pseudomonas spp***. to Tobramycin (28.3 %, p = 0.007) was significantly high in the patients under the age category of adults classified by WHONET software.

Although it is difficult to determine what factors cause some bacteria to become resistant to one antibiotic but not others, a study found a link between fluoroquinolone antibiotic resistance and patient age, with the rate of antibiotic resistance to fluoroquinolones increasing as the patient's age increases. Other antibiotic classes, such as penicillins and macrolides, did not show this trend, with either a high or low risk of antibiotic resistance independent of patient age. In addition, concerning the fluoroquinolone family, as the patient's age increases, the number of multiple-resistant isolates likewise increases. This pattern is characterized by norfloxacin resistance in the first decade of life, increased resistance to ciprofloxacin, levofloxacin, and ofloxacin in the fourth decade, and finally, resistance to moxifloxacin and gatifloxacin at a later age, acquiring multiple resistances to all members of the fluoroquinolone family,[41] which is consistent with our findings that *S. aureus* is resistant to ciprofloxacin among adults. In the present study, MRSA was the most prevalent species. Kot *et al*,[42] in their study, reported that resistance to levofloxacin (83.9%), ciprofloxacin (83%), erythromycin (77.7%), and clindamycin (72.3 %) was found in a substantial majority of MRSA isolates and 92.9% of MRSA isolates were multidrug-resistant (MDR) in the study. Therefore, it was observed that the most common resistance pattern among MDR MRSA isolates included resistance to erythromycin, clindamycin, ciprofloxacin, and levofloxacin. In the present study, the majority of the *E. coli* were from the urine isolates and *E.coli* resistance to Amoxicillin/Clavulanic acid was high among adults 68.4 % (n = 26/38). These findings contradicted those of Salama *et al*,[43] who found a significant level of *E. coli* resistance to Amoxicillin/Clavulanic acid in their investigation among children from 1 to 5 years of age with Urinary Tract Infection (UTI). Pneumonia and other respiratory infections are routinely treated with ceftriaxone. It's a first-line antibiotic for community-acquired pneumonia and a fluoroquinolone option for penicillin-resistant isolates. *Klebsiella* and *E. coli* strains were the first to be identified as having ESBLs (Extended Spectrum Beta Lactamases).In a study conducted by Bushra *et al*,[44]*Klebsiella pneumoniae* showed the highest resistance against

ceftriaxone among other pathogens. Piperacillin-tazobactam is a β-lactam/β-lactamase inhibitor (BL/BLI) that is often used to treat Enterobacteriaceae infections. Resistance to piperacillin-tazobactam in these bacteria is generally produced by enzymes that hydrolyze piperacillin and are not sufficiently inhibited by tazobactam, such as carbapenemases, AmpC-lactamases, and some extended-spectrum-lactamases (ESBLs). Most Enterobacteriaceae that are resistant to piperacillin/Tazobactam are also resistant to ceftriaxone because such enzymes hydrolyze third-generation cephalosporins (ceftriaxone). Ryu *et al*,[45] in their study reported that the rate of resistance to piperacillin/tazobactam in *K. pneumoniae* increased significantly over the study period (2012 to 2016).In the present study, the resistance for ***Pseudomonas spp.*** is significantly high among pediatric patients to Nitrofurantoin (40 %, p = 0.017).In an Iranian study, hospitalized children with urinary tract infections were given chemoprophylaxis with trimethoprim/sulfamethoxazole, nitrofurantoin, or cephalosporins. The pattern of antibiotic resistance was observed according to the antibiotic used; nitrofurantoin was resistant to 100% of Pseudomonas spp. Isolates.[46]

Table No. 3: The resistance pattern of the most prevalent bacteria among the in-patients concerning gender

Organisms	**Male** (%) n	**Female**(%) n	p-value	Antibiotics
S. aureus	**20.4 (47/230)**	**27 (62/230)**	**0.035**	**Trimethoprim/ Sulfamethoxazole**

From the Table 3 which shows the resistance pattern of the most prevalent bacteria among the in-patients concerning gender, it was evident that ***Staphylococcus aureus*** from female patients was found to be significantly more resistant to Trimethoprim/Sulfamethoxazole (27%, p = 0.035). These findings were consistent with the study conducted by Dilnessa *et al*,[47]where MRSA strains were 100 % resistant to trimethoprim/sulfamethoxazole in which majority of the study participants were females (51.9 %) compared to males (48.1 %).

Table 4 highlights the resistance pattern of the most prevalent bacteria among the in-patients concerning location. The most prevalent uropathogen in children is *E. coli*. Trimethoprim-sulfamethoxazole, despite its widespread usage, due to significant resistance rates in many areas, is not a good option as an empirical antibiotic of choice for the treatment of urinary tract infections in children.

Table No. 4: The resistance pattern of the most prevalent bacteria among the in-patients concerning location

Organisms	Dermatology, Venereology, and Leprosy (%) n	ENT (%) n	Medicine (%) n	Obstetrics & Gynecology (%) n	Orthopedics (%) n	Pediatrics (%) n	Plastic Surgery (%) n	Surgery (%) n	Urology (%) n	p-value	Antibiotics
E. coli	0.5 (1/189)	0	12.1 (23/189)	12.7 (24/189)	0.5 (1/189)	17 (32/189)	1.6 (3/189)	14.8 (28/189)	0	0.042	Trimethoprim/ Sulfamethoxazole
Klebsiella sp.	0	0	4.4 (7/160)	3.1 (5/160)	1.9 (3/160)	1.9 (3/160)	0.6 (1/160)	3.1 (5/160)	0	0.003	Amikacin
	1.1 (1/90)	2.2 (2/90)	44.4 (40/90)	14.4 (13/90)	3.3 (3/90)	7.8 (7/90)	0	22.2 (20/90)	0	0.000	Ampicillin
Pseudomonas sp.	0	0	3.3 (4/123)	4.1 (5/123)	2.4 (3/123)	4.1 (5/123)	4.1 (5/123)	13 (16/123)	0	0.052	Ciprofloxacin
	0	0	2.1 (3/141)	0.7 (1/141)	0.7 (1/141)	2.1 (3/141)	0.7 (1/141)	1.4 (2/141)	0.7 (1/141)	0.028	Piperacillin/ Tazobactam

In the present study, it was observed that ***Escherichia coli*** isolates from the Pediatric ward were found to be significantly more resistant to Trimethoprim/Sulfamethoxazole (17 %, p = 0.042). These findings were consistent with the study conducted in India where *E. coli* exhibited the highest resistance toward Trimethoprim/Sulfamethoxazole (83.3 %).[48]***Klebsiella spp.*** isolates from the Medicine ward were found to be significantly more resistant to Amikacin (4.4 %, p = 0.003) and Ampicillin (44.4 %, p = 0.000). Similar findings were reported by P. Aminul *et al*,[49] where clinical isolates of *Klebsiella pneumoniae* were resistant to most β – lactam antibiotics and aminoglycosides (Amikacin – 50.3 %).On the contrary, Amikacin was 100 % susceptible to *Klebsiella pneumoniae* isolates but 78.3 % resistant to Ampicillin in a study conducted by Ayatollahi *et al*,[50] in Iran. Ciprofloxacin is the commonly prescribed definitive antibiotic therapy in the surgery ward of the hospital. *Pseudomonas aeruginosa*, an opportunistic bacterium, is routinely treated with the antibiotic ciprofloxacin. Because of its extensive use, the number of P. aeruginosa isolates that are resistant to ciprofloxacin is rapidly increasing. In the present study, ***Pseudomonas spp.*** isolates from the Surgery ward was found to be significantly more resistant to Ciprofloxacin (13 %, p = 0.052).Also, the *Pseudomonas spp.* isolates from the Medicine ward and Pediatric wards were found to be significantly more resistant to Piperacillin/ Tazobactam (2.1 %, p =

0.028). These findings were consistent with the study conducted by Carmeli *et al*,[51]which was conducted to compare the emergence of resistance in Pseudomonas aeruginosa to four anti-pseudomonal agents' ceftazidime, ciprofloxacin, imipenem, and piperacillin in which ciprofloxacin was the most resistant (21 %) followed by imipenem (13 %), ceftazidime (7 %) and piperacillin (5 %).

The rising frequency of antibiotic resistance in both health care and community settings poses a formidable problem as hospitalized patients get increasingly complex to treat. The future of effective antimicrobial therapy is bleak, given the increasing complexity of illnesses and the scarcity of new antimicrobials in development. Antibiotic stewardship increasingly recognizes continuous surveillance of local antimicrobial susceptibility patterns as a crucial element in fighting growing antimicrobial resistance. The findings of this study support the necessity for Antimicrobial Stewardship Programs to be implemented across the clinical practice to ensure standardization of antibiotic use across the institution. In order to create shared knowledge and widespread practice diffusion, successful ASPs should prioritize collaboration among all healthcare practitioners. Support from hospital administration and collaboration among pharmacy, infectious disease specialists, and clinical microbiologists are the cornerstones of a successful stewardship Programme. Efforts should consequently be directed toward infection prevention through the implementation of Stewardship programs. This is especially critical in the fight against AMR.

The present study is one of the few to use WHONET software to create an institutional antibiogram in an Indian setting to monitor antibiotic resistance and stratification of antibiograms. Because it is based on a retrospective dataset, the present study has substantial limitations. Though the hospital delivers good clinical and laboratory services and maintains accurate record, retrospective data can't be relied upon to reach the same high standards as a prospective study. Patients admitted to the ICU and outpatients were excluded. This may limit the generalizability of our findings. Furthermore, it was carried out at a single-center, public tertiary teaching hospital in southern India, external validity is a constraint.

CONCLUSION:

The current study provides insight into the regional trend of antibiotic resistance.In conclusion, with the increasing prevalence and resistance of ESKAPE pathogens, it is necessary to institutionalize Antimicrobial Stewardship Programs with hospital-specific rules. The antimicrobial policy should be one of the obligatory requirements in every healthcare

setting, and formulating an antibiogram has to be the first step before defining an antibiotic policy. Our findings will aid in the establishment of antibiotic policy and the selection of empiric therapy options. We could observe significant differences in the antibiotic susceptibility patterns to bacterial isolates among inpatients in different wards of the hospital. Therefore, we recommend the development of stratified antibiograms based on individual units or wards of a hospital which provides a more accurate view of bacterial susceptibility patterns besides ensuring clinical confidence in the prescription of empiric therapy.

ETHICAL CLEARANCE:

This study was approved by Institutional Human Ethics Committee, Number: IHEC/721/2021 dated 04th August 2021, and permitted by the Member Secretary, Institutional Human Ethics Committee, Rajah Muthiah Medical College, and Hospital, Annamalai University. The registration number of IEC is EC/NEW/INST/2020/1249. Participants' informed consent was not required. No human participants were used in this investigation, and there was no consent process.

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DATA AND MATERIALS AVAILABILITY:

The corresponding author and the hospital's microbiology department have all relevant data, which they can provide upon reasonable request.

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AUTHOR CONTRIBUTIONS:

Conceptualization and methodology including data collection: HBJ, AM, RSSR, MS and KJ; Writing – Original draft preparation and literature search: HBJ, AM, RSSR; Writing – review and supervision: MS and KJ. The final manuscript has been read and approved by all the authors.

CONFLICT OF INTEREST:

The authors affirm that the publishing of this paper is free of conflicts of interest.

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