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PATTERNS OF ANTIBIOTICS AND RESISTANCE IN A TERTIARY CARE HSOPITAL

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ABSTRACT:

Patients in critical condition are more likely to get infections caused by different antibiotic-resistant microorganisms. This goal of the study was to identify the common isolates and the patterns of antibiotic resistance in these patients. 794 samples throughout were examined and 18% of the samples had growth, producing 143 organisms. Pseudomonas sp, Acinetobactersp, Escherichia coli, and Klebsiellasp, Staphylococcus sp, Enterobactersp, Enterococcus sp, Proteussp, and Serratia sp. were the main organisms isolated. There were more than 50% of third generation cephalosporin-resistant E. coli, Pseudomonas, Proteus and Acinetobacter strains. Colistin, tigecycline, carbapenems, and quinolones were evidently sensitive to the majority of the identified pathogens. All significant isolated organisms were resistant to cephalosporins, penicillins, and aminoglycosides.

Keywords: Antibiotic resistant, Acinetobacter, Proteus, Pseudomonas, Enterococcus, Serratia, Colistin, Tigecycline, Carbapenem, Cephalosporin-resistant, Penicillin-resistant.

ISSN PRINT 2319 1775 Online 2320 7876
Research paper Volume 11,Spl Iss 3, 2022

INTRODUCTION:

Modern medicine is built on the foundation of antibiotics. Antibiotic resistance is a hazard to humanity and a global public health issue.[1]India has the greatest rate of infectious disease burden worldwide, and recent studies have shown that using antibiotics indiscriminately and unnecessarily to treat illnesses has increased the emergence of antibiotic resistance (AMR).[2]AMR has become a major problem in India due to a lack of funding, poor infrastructure, a high illness burden, and uncontrolled sales of cheap antibiotics.[3]Hospitalizations are frequently caused by bacterial infections, and critical care environments are particularly prone to nosocomial infections.[4]

The growth of antibiotic resistance and the scarcity of effective treatments globally provide a growing issue for the control of bacterial illnesses. The percentage of nosocomial infections among ICU patients ranges from 5% to 30%. A patient's sickness severity, length of exposure to invasive devices and procedures, frequency of contact with healthcare professionals, and length of hospital stay are all linked to an elevated risk of infection. Infections brought on by gram-positive organisms have been the focus of infection management strategies and novel antibiotic developments for the past 15 to 20 years.[5,6,7]

Gram-negative bacterial infections have become more common in intensive care units (ICU) followed by departments, and the scarcity of treatments for some MDR strains is concerning. MDR gram-negative bacterial infections are known to have substantial morbidity and fatality rates.[8] In order to enhance patient outcomes and save hospital costs, infection control and infection treatment protocols should be carefully followed.

A significant public health concern, AMR, which occurs when a pathogen can withstand exposure to antibiotic therapy. In poor nations like India, where infectious diseases still have a high morbidity and mortality rate, infection control would be a challenging task.[9,10]For the development of resistance, which cannot be reduced once developed even by limiting the use of antibiotics, a number of intrinsic factors, including point mutation and gene amplification, and extrinsic factors, such as horizontal transfer of resistant genes between bacteria within and across species by transposons, integrins, or plasmids, have been postulated. The rise of AMR has been

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attributed to social causes including population changes, poor hygiene practices, and overcrowding.

Based on the findings of various cultures of microbiological specimens from hospitalized patients, we analyze the pattern of prevalence of organisms, antibiotic sensitivity and resistance in this study.

MATERIALS AND METHODS:

Site of the study: The study was conducted in a tertiary care hospital, Hyderabad.

Study Design: The study was prospective observational study.

Duration of the study: The duration of the study was eight months.

Source of data: The source of data was patient collection forms, medical records, case sheets, microbiology registers, culture sensitivity results and laboratory investigations.

Inclusion criteria:

- Patients with infections.
- Patients with positive culture and sensitivity reports.
- Patients aged above 20 years.
- Patients with known comorbidities.
- Patients willing to participate.

Exclusion criteria:

- Patients below 20 years of age.
- Pregnant and lactating women.

Study Methodology:

Isolation and Identification:

Clinical samples from the selected patients were obtained in sterile containers, and then, in accordance with established methods in the laboratory, bacteria were isolated and identified from the specimens. The rest of the clinical specimens were inoculated onto blood agar and cysteine lactose electrolyte deficient (CLED) using a calibrated wire loop (0.001 mL), and then incubated

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overnight at 37 °C. The blood samples were placed into aerobic culture media.Due to their hemolytic activity, Gram-positive bacteria were cultured and identified using blood agar, and whereas Gram-negative bacteria were cultured and identified using CLED due to their capacity for lactose fermentation.The threshold for significant colony counts was 105 colony-forming units per milliliter (CFU/mL). Culture plates that showed no bacterial growth underwent a second 48-hour incubation.

Depending on the type of recovered microorganisms, Gramm staining, morphological characterization, and various biochemical tests were used to confirm the identification of the bacteria. For example, the catalase reaction, slide and tube coagulase tests, culture on DNase agar, and bile esculin were used to identify Gram-positive bacteria, while oxidase, triple sugar iron, motility indole ornithine, citrate, lysine.

Data collection and analysis:

Results of clinical specimens such as blood, urine, respiratory secretions, pus/wound swabs, cerebrospinal fluid, and sputum collected during the study period that were tested for antibiotic susceptibility were included in the study. The microbiology registers, patient demographics and data on culture (identification) and sensitivity results were also recorded. A pre-designed data abstraction tool and Microsoft Excel was used to collect the data. Following a basic descriptive examination of the resistance profiles of isolated organisms, the entered data were validated for accuracy and completeness.

RESULTS:

Numerous variables play a role, including the ageing of patients, the availability of extensive surgical and rigorous medicinal interventions for the treatment of previously incurable diseases, and the widespread use of antibiotics that can choose a resistant microbial flora.

Table-1: Demographics

Parameters	**No of Subjects**
Gender	
Male	78 (54.5%)
Female	65 (45.5%)

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Age (in years)	
<20	9 (6.6%)
20-40	22 (15.4%)
40-60	29 (20.5%)
>60	83(57.5%)
Comorbidities	
Hypertension	15 (10.5%)
Diabetes Mellitus	35 (25)
Cardiovascular Diseases	27 (18.9%)
Renal Disorders	52 (36.4%)
Hepatic Disorders	9 (6.3%)
Immunocompromised patients	5 (3.5%)

From the study, the prevalence of male was 54.5% i.e. 78 subjects followed by 45.5% of females i.e. 65 subjects. More number of subjects were observed in age group of >60 years i.e. 83 (57.5%) subjects, followed by 29 (20.5%) subjects in the age group of 40-60 years, 22 (15.4%) subjects in the age group of 20-40 years, and 9 (6.6%) subjects in the age group of <20 years.

Majority of subjects had renal disorders i.e. 52 (36.4%) subjects followed by diabetes mellitus i.e. 35 (25%) subjects, cardiovascular disorders i.e. 27 (18.9%) subjects, hypertension i.e. 15 (10.5%) subjects, hepatic disorders i.e. 9 (6.3%) subjects, and immunocompromised patients were 5 (3.5%) subjects.

ISSN PRINT 2319 1775 Online 2320 7876
Research paper **Volume 11,Spl Iss 3, 2022**

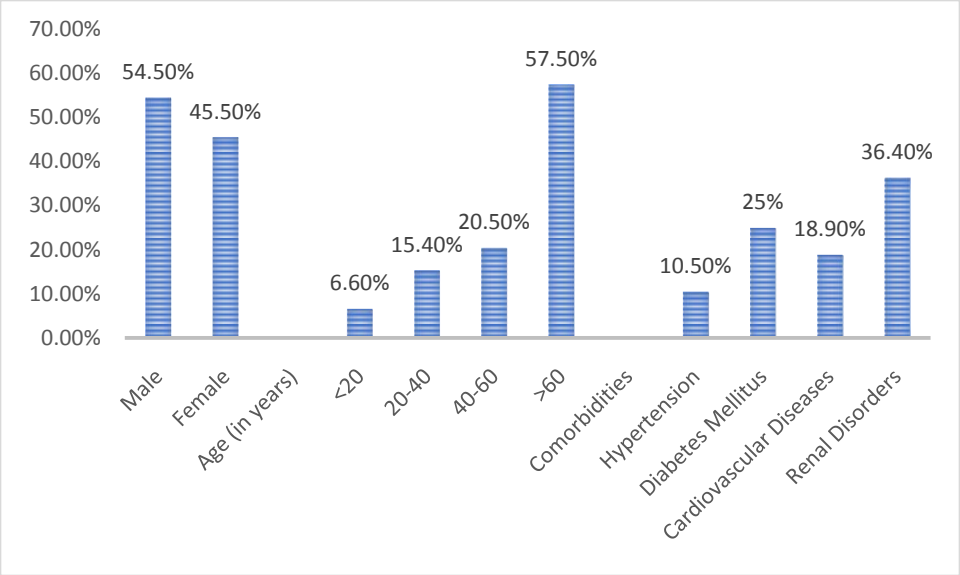

Figure-1: Gender, age and comorbidities of the subjects

Table-2: Samples used for culture sensitivity tests

Sample	**No of subjects**
Blood	44 (30.8%)
Urine	60 (42%)
Respiratory secretions	21 (14.7%)
Pus/Wound swabs	8 (5.6%)
Sputum	10 (7%)

Various samples were used to isolate the bacteria. Majority of urine samples were used for culture sensitivity tests i.e. 60 (42%) subjects, followed by blood samples that were 44 (30.8%) subjects, samples for respiratory secretions were 21 (14.7%) subjects, sputum samples were 10 (7%) subjects, and samples from pus/wounds swab were 8 (5.6%) subjects.

ISSN PRINT 2319 1775 Online 2320 7876
Research paper Volume 11,Spl Iss 3, 2022

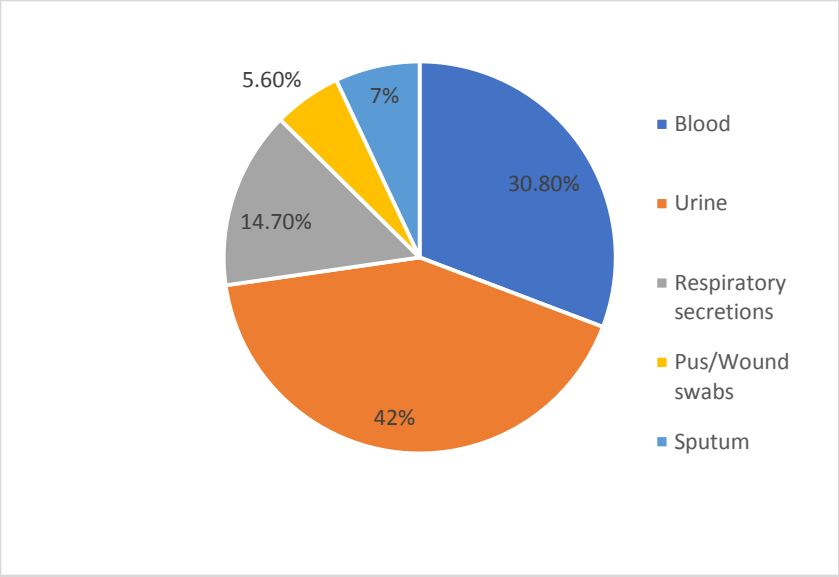

Figure-2: Sample used to isolate organisms

Table-3: Organism isolated from cultures

Organism	**No of subjects**
Acinetobacterbaumanni	21 (20.7%)
Pseudomonas aeruginosa	24 (16.5%)
Escherichia Coli	38 (26.4%)
Klebsiella pneumonia	23 (16.3%)
Enterobacter	2 (1.4%)
Serratiamarcenes	3 (2.2%)
Staphylococcus aureus	4 (2.8%)
Proteus mirabalis	1 (0.7%)
Enterococcus faecum	13 (9%)
Morganellamorganii	3 (2.2%)
Streptococcus pneumonia	8 (5.6%)
Enterococcus faecalis	3 (2.2%)

After the culture sensitivity test from various samples, various isolates were found. Major of isolate found was Escherichia coli i.e. 38(26.4%) subjects, followed by 21 (20.7%) subjects with

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Acinetobacterbaumanni, 24 (16.5%) subjects with pseudomonas aeruginosa, 23 (16.3) subjects with klebsiella pneumonia, 13 (9%) subjects with enterococcus faecum, 8 (5.6%) subjects with streptococcus pneumonia, 4 (2.8%) subjects with staphylococcus aureus, 3 (2.2%) subjects with serratiamarcenes, morganellimorganii, and enterococcus faecalis each, 2 (1.4%) patients with enterobacter, and 1 (0.7%) subjects with protuesmirabalis.

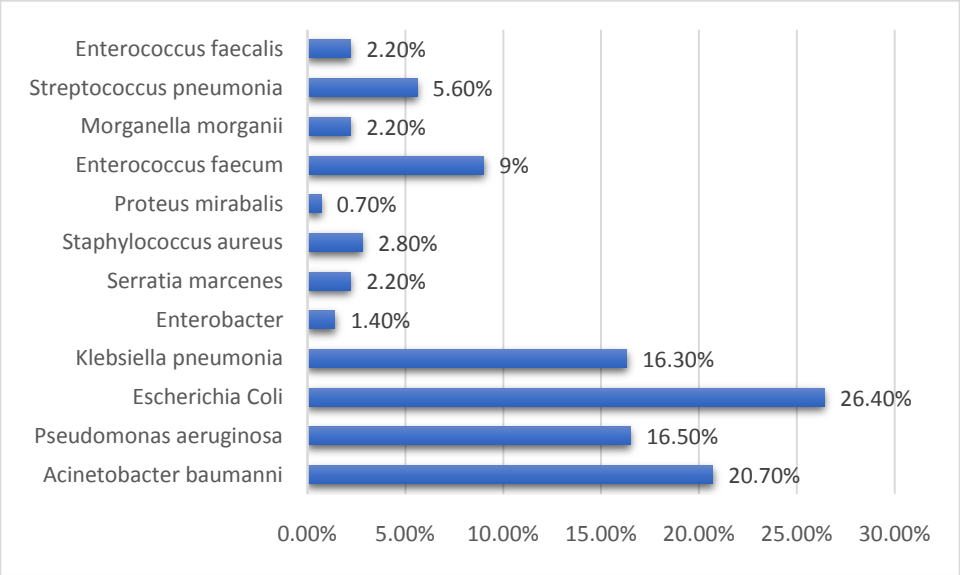

Figure-3: Prevalence of organisms isolated from cultures

Table-4: Length of hospital stay

No of days	**No of subjects**
<10	24 (16.8%)
11-15	58 (40.6%)
16-25	44 (30.8%)
>26	17 (11.9%)

The above table represents the data on length of hospital stay. Majority of the subjects i.e. 58 (30.8%) had the duration as 11-15 days, followed by 44 (30.8%) subjects with duration as 16-25 days, 24 (16.8%) subjects with <10 days, and 17 (11.9%) with >26 days.

ISSN PRINT 2319 1775 Online 2320 7876
Research paper Volume 11,Spl Iss 3, 2022

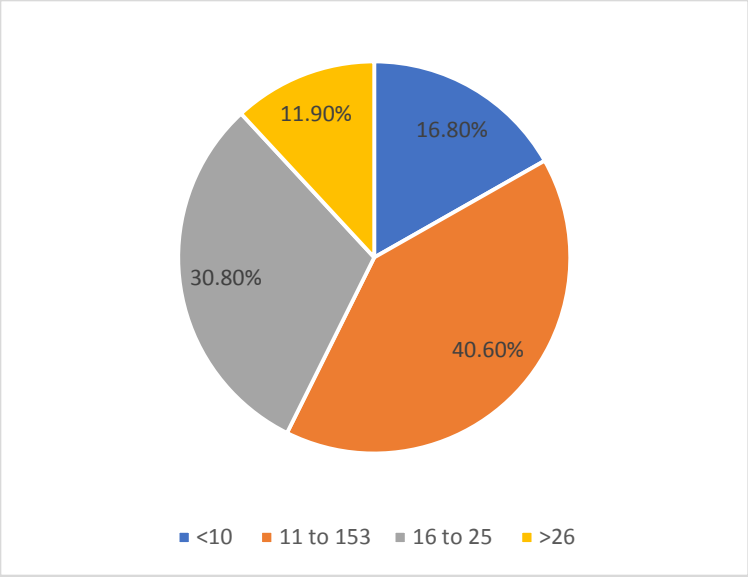

Figure-4: Number of days of hospitalization in subjects

Table-5: Antibiotics used.

Antibiotics	**No of subjects**
Amikacin	6 (4%)
Gentamycin/Tobramycin	9 (6%)
Tigecycline	40 (28%)
Cefepime	11 (8%)
Ceftazidime	3 (2%)
Cefotaxime	5 (3.4%)
Ceftriaxone	9 (6.3%)
Imipenem	10 (7%)
Meropenem	12 (8.3%)
Colistin	28 (20%)
Levofloxacin	1 (0.7%)
Ciprofloxacin	1 (0.7%)
Vancomycin	2 (1.4%)
Rifampin	1 (0.7%)
Piperacillin-Tazobactum	5 (3.5%)

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The above table represents the data on antibiotics used in the treatment. Amikacin was used in 6 (4%) subjects, Gentamycin/Tobyamycin was used in 9 (6%) subjects, Tigecycline in 40 (28%) subjects, cefepime in 11 (8%) subjects, ceftazidime in 3 (2%) subjects, cefotaxime in 5(3.4%) subjects, ceftriaxone in 9 (6.3%), imipenem in 10 (7%) subjects, meropenem in 12 (8.3%), colistin in 28 (20%) subjects, levofloxacin in 1 (0.7%) subject, ciprofloxacin in 1 (0.7%) subjects, vancomycin in 2 (1.4%) subjects, rifampin in 1 (0.7%) subjects and piperacillin-tazobactum in 5 (3.5%) subjects.

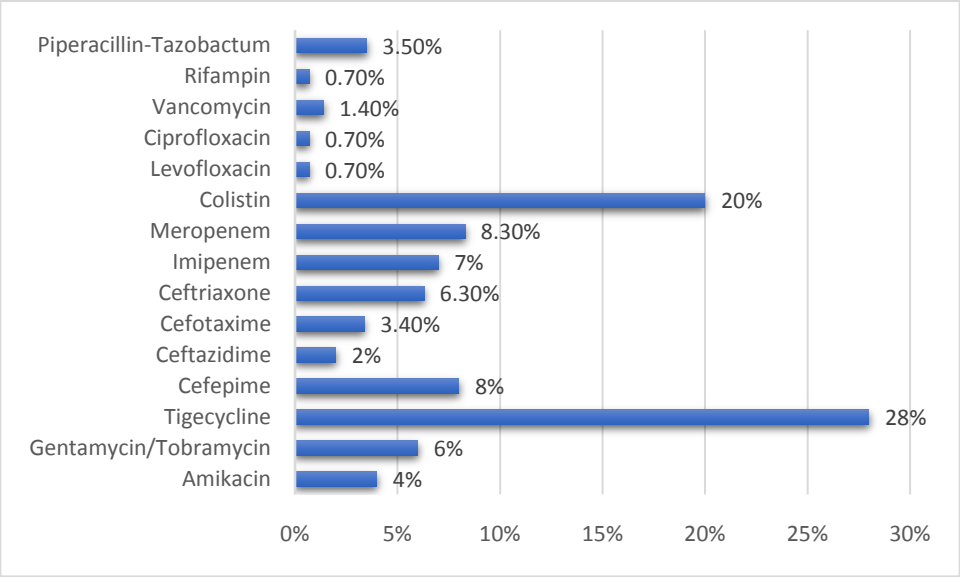

Figure-6: Antibiotics used to treat subjects.

Table-7: Resistant patterns

Organism	**Sensitive**	**Resistant**
Acinetobacterbaumanni	Colistin (21.2%) Tigecyclin (44.8%)	Piperacillin (77.2%), Cephalosporins (54.3%), Aminoglycosides (67.2%)
Pseudomonas aeruginosa	Carbapenem (34.5%), Quinolones (67.1%).	Piperacillin (89.1%), Cephalosporins (44%), Aminoglycosides (81.9%).
Escherichia Coli	Colistin (11.9%), Tigecyclin (65.7%),	Piperacillin (68.5%), Cephalosporins (57.8%),

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	Nitrofurantoin (23.9%), Carbapenems (18.4%).	Aminoglycosides (21.9%)
Klebsiella pneumonia	Amikacin (21.7%), Cephalosporins (34.9%), Carbapenem (11.5%), Tigecycline (16.8%), Vancomycin (12.4%).	Penicillin (82.9%), Tetracycline (42.2%), Quinolone (21.2%).
Enterobacter	Aminoglycoside (62.1%), Quinolone (21.7%), Carbapenem (9.8%)	Piperacillin(67.9%), Cephalosporins (23.5%).
Serratiamarcenes	Penicillin (55.2%), Quinolones (41.4%), Colistin (24.8%).	Clarithromycin (43.2%), Erthromycin (21.8%), Cotrimoxazole (28.6%)
Staphylococcus aureus	Carbapenem (36.2%), Rifampin (19.6%), Quinolone (7.4%).	Penicillin (76.1%), Vancomycin (28.2%), Clindamycin (8.3%)
Proteus mirabalis	Tetracycline (54.7%), Quinolones (11.9%).	Colistin (52.7%), Piperacillin (27.4%), Cephalosporins (56.9%).

Above table represents the data on resistant patterns of different antibiotics in accordance with the organisms isolated. For *Acinetobacterbaumanni*, Colistin (21.2%) and Tigecycline (44.8%) were found to be sensitive. Piperacillin (77.2%), Aminoglycosides (67.2%),Cephalosporins (54.3%) were found to be resistant.

For *Pseudomonas aeruginosa*, Carbapenem (34.5%), and Quinolones (67.1%) were found to be sensitive. Piperacillin (89.1%), Aminoglycosides (81.9%), Cephalosporins (44%) were found to be resistant.

For *Escherichia Coli*, Colistin (11.9%), Nitrofurantoin (23.9%), Carbapenems(18.4%), Tigecycline (65.7%) were sensitive. Piperacillin (68.5%), Cephalosporins (57.8%), Aminoglycosides (21.9%) were resistant.

ISSN PRINT 2319 1775 Online 2320 7876
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For *Klebsiella pneumonia*, Cephalosporins (34.9%), Amikacin (21.7%), Tigecycline (16.8%), Vancomycin (12.4%), Carbapenem (11.5%) were sensitive. Penicillin (82.9%), Tetracycline (42.2%), Quinolone (21.2%) were resistant.

For *Enterobacter*, Aminoglycoside (62.1%), Quinolone (21.7%), Carbapenem (9.8%) were found sensitive. Piperacillin (67.9%), Cephalosporins (23.5%) were resistant.

For *Serratiamarcenes*, Carbapenem (36.2%), Rifampin (19.6%), Quinolone (7.4%) were sensitive. Penicillin (76.1%), Vancomycin (28.2%), Clindamycin (8.3%) were resistant.

For Proteus mirabalis, Tetracycline (54.7%), Quinolones (11.9%) were sensitive and Cephalosporins (56.9%),Colistin (52.7%), Piperacillin (27.4%) were resistant.

It is clearly evident that cephalosporins, penicillins, and aminoglycosides were resistant to all major isolated organisms. Colistin, tigecycline, carbapenems and quinolones were sensitive to most of the isolated organisms.

Table-8: Outcomes

Outcome	**No of patients**
Discharge	97 (68%)
LAMA	37 (25.9%)
Death	9 (8.6%)

The above table represents the data on outcomes. 97 (68%) subjects were discharged, 37 (25.9%) had LAMA and 9 (8.6%) died.

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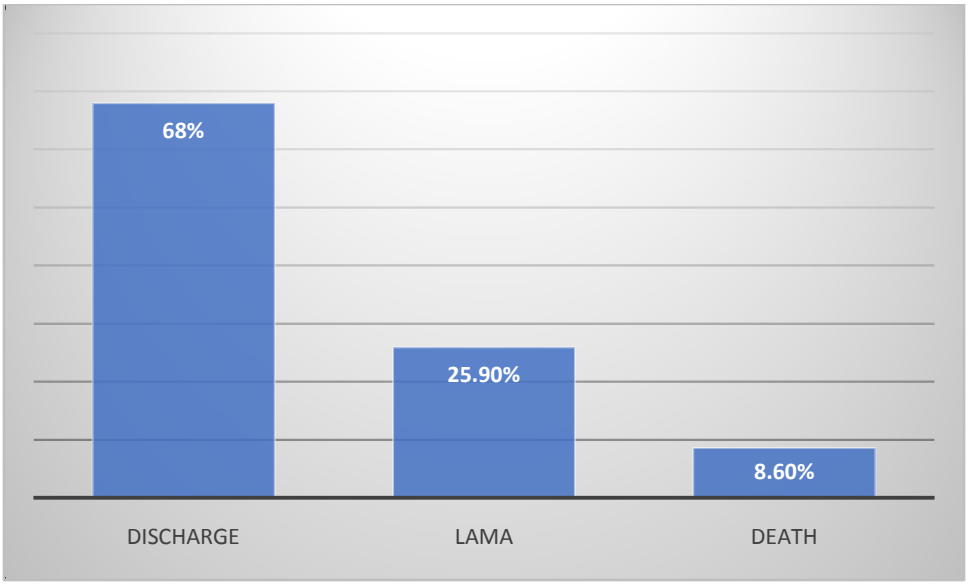

Figure-8: Outcomes of the subjects.

DISCUSSIONS:

The 'wonder medications' for fighting microorganisms are antibiotics. Numerous antibiotic types have been utilized for medicinal purposes for many years. Uncertainty has developed as a result of microorganisms developing resistance to popular antibiotics without the host's knowledge. Antibiotic resistance is growing alarmingly quickly. A growing number of illnesses, such as pneumonia, TB, and gonorrhoea, are becoming more challenging and occasionally impossible to treat, while medications are losing their efficacy and devolping resistance. Infections that are resistant to antibiotics are correlated with the irrational antibiotic use. High morbidity and mortality rates are reported as a result of the restricted antibiotic treatment options available for persistent or newly emergent difficult-to-treat multidrug resistant bacterial infections.[11]

In critically ill patients, antibiotic resistance is an increasingly prevalent concern that has an impact on the patients' prognosis and chance of survival.Additionally, it leads to a longer hospital stay, which raises the expense of care.[12]

Maximum resistance, according to Saravanan R et al[13], was seen with first-line antibiotics that are frequently used, including co-trimoxazole, ampicillin, amoxicillin, amoxyclav, fluoroquinolones, third-generation cephalosporins, and nalidixic acid. Among the gram-negative bacteria, amikacin, nitrofurantoin, gentamycin, and doxycycline had the lowest resistance or

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highest sensitivity. Vancomycin, macrolides, gentamycin, nitrofurantoin, and clindamycin were the antimicrobials that were most responsive to gram-positive bacteria.

Chakravarthi et al.'s study[14]reported Gram-negative bacteria made up 58% of these, gram-positive bacteria made up 27%, and fungal growth was seen in 15% of the samples. Blood (n = 48), urine (n = 39), ET aspirate (n = 40), central venous catheter tips (n = 4), sputum (n = 17), and pus (n = 11) were among the samples sent for culture.In a study by Savanur SS et al[12],E. coli, Klebsiella, Acinetobacter, and Pseudomonas were the most frequently isolated microorganisms (18.6%, 11.6%, 14.5%, and 9.8% respectively). This is consistent to other research where the most typical isolates were gram-negative microbes.[8]

According to a study conducted in an Indian intensive care unit, Acinetobacter sp., Escherichia coli, Klebsiella sp., Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pyogen, etc. were the most prevalent microorganisms.[15]However, in an ICU in Europe, coagulase-negative staphylococcus (19.1%), yeast (17.1%), Pseudomonas aeruginosa (28.7%), and Staphylococcus aureus (30.1%) were the most frequently isolated organisms.[16]

Every day, bacterial illness treatments became more aggressive. As antibiotics become less effective, infections persist; treatment failure is frequently caused by antibiotic and multi-drug resistance, as is the case with diseases like tuberculosis. There is a need for more recent and potent antibiotics that have no known bacterial resistance. In order to combat bacterial infection, several treatment approaches are being considered. It has been proven successful to prevent bacterial infections using passive immunization or the delivery of antibodies to non-immunized individuals.[17]Phage treatment, in which bacteriophages are utilized to treat pathogenic bacterial infections, is another successful intervention.[18] To combat antibiotic resistance, numerous novel classes of antimicrobials are currently undergoing clinical trials.[19] Intervention approaches target biological networks rather than just targets in an effort to develop new antibacterial treatments.[20] Combination therapy that combine antibiotics and antibiotic-enhancing phage have shown promise as antimicrobial interventions.[21]

For better clinical decision-making regarding the start of empirical antibiotics with antibiotic stewardship programmes, which are helpful in preventing the emergence of MDR and extremely drug resistant organisms, a local antibiogram probably needs to be drawn in every ICU setup at

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this point, at least quarterly. The use of broad-spectrum empirical antimicrobials along with strong de-escalation techniques is crucial in this case to reduce collateral damage to both present and future patients. To minimize nosocomial infections and improve patient response and clinical outcomes, emphasis should also be placed on the use of sterile methods while inserting equipment, hand cleanliness, and the use of gowns and gloves in the intensive care unit (ICU).

CONCLUSIONS:

Antibiotic resistance is a significant emerging issue in contemporary clinical practice, posing new difficulties for treating physicians and placing a significant cost burden on patients who are bystanders. In ICU settings and departments, drug resistant infections are on the rise, which raises morbidity and death. In order to start empirical antibiotics in emergency situations, it is necessary to conduct timely antibiogram and antibiotic stewardship programmes for a better understanding of the type of organism, their sensitivity, and their pattern of resistance. De-escalation of antibiotic use must also be emphasized wherever necessary in order to stop further antibiotic overuse and the development of antibiotic resistance in these organisms. Better drug use results in better preservation of supplies for upcoming generations. AMR was more prevalent among hospital acquired pathogens and against widely used, long-established antibiotics. It is determined how resistance and sensitivity patterns change over time and in different places. Antibiotic rotation and routine AMR monitoring are advised to stop the spread of resistance.

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