

A PROSPECTIVE OBSERVATIONAL STUDY TO ASSESS THE USE OF RESTRICTED ANTIBIOTICS AND ADHERENCE TO THE ANTIBIOTIC POLICY AT A TERTIARY CARE

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ABSTRACT

The majority of developing nations have implemented antibacterial policies to address the grave issue of drug resistance. The purpose of this study was to prospectively identify the compliance with the antibiotic policy in various hospital treatment departments and potential causes of non-compliance. The aim was to examine how often restricted antibiotics are used in each inpatient department and to ensure that the Hospital's antibiotic policy is followed. The study involved a prospective examination of hospital patient files. The most recent hospital admissions' clinical notes and prescription records were examined for antibiotic prescribing. Patients were watched until release while hospital computer reports on culture and sensitivity were secured. Observations were made and meticulously recorded. Out of 150 prescriptions included in the study, 84 (56%) patients were male and 66 (44%) patients were female; the most prevalent diseases for which restricted antibiotics are used were 4 (11.70%), UTI 3 (8.12%), and SEPSIS 27 (79.41%). The limited antibiotic that is most usually prescribed is piperacillin-tazobactam (46.7%). C/S testing was done on 93 (62% of the patients). Klebsiella 14 (25%) was the most often seen organism, followed by E. coli 10 (17.8%) and staphylococcus aureus 6 (10.71%). In 105 cases (or 70%), hospital policy was followed. 22/150 (14.66%) prescriptions had an ADR. There was low adherence to hospital antibiotic policy. Physicians' antibiotic prescribing practises should be optimized. Adherence to and update of the policy is recommended.

INTRODUCTION

A natural substance that kills bacteria, such as specific forms of mould or compounds produced by living creatures, was formerly referred to as a "antibiotic." Although many people use the term "antibiotic" to apply to both natural and artificial (man-made) substances, the term "antimicrobial" technically pertains to both. Only anaerobic bacteria can be successfully treated with a broad-spectrum antibiotic. Anaerobic bacteria do not require oxygen while aerobic bacteria do. Antibiotics may occasionally be administered in order to avoid an infection rather than to treat one, such as before surgery. This is referred to as "prophylactic" antibiotic usage. Common applications include orthopaedic surgery [1]. The majority of antibiotics work against an infection within a few hours. To prevent the infection from returning, it's crucial to finish the entire course of treatment. Of course, stopping the medicine early increases the likelihood that the germs will develop resistance to subsequent treatments. This is due to the fact that those that survive have been exposed to the antibiotic in some capacity and may as a result have developed a resistance to it. Even if a patient feels better, they must finish the prescribed course of treatment [2]. Bacterial evolution under the selective pressure of antimicrobial use, including the selection of antimicrobial therapy, the length of therapy, the mode of administration, and the dosage, is a significant contributor to the emergence of drug-resistant bacteria. When an antibiotic is administered to a patient, the likelihood that they will become colonised or infected with a resistant bacterium rises. The prevalence of resistant bacteria in hospitals has increased as a result of increased use of antimicrobials. Increases in morbidity and death are linked to infections caused by resistant bacteria, notably the C. difficile epidemic strain and Methicillin-resistant Staphylococcus aureus (MRSA) [3]. Given its financial and staffing limitations, every hospital should make the most of its resources to put up a successful team. A successful programme requires close cooperation between the administration, hospital epidemiology, and the microbiology lab staff. In the case of implementing the programme in a hospital context, a working relationship with the information expert might be extremely beneficial [4].

The following are the objectives of the antibiotic stewardship programme:

The "4 Ds" of ideal antibiotic administration. Right medication, dosage, de-escalation to pathogen-directed therapy, and length of therapy are all important factors.

to stop the misuse, abuse, and overuse of antibiotics.

limit the emergence of resistance in patients as a whole as well as in the community [4].

Principal methods for antimicrobial stewardship:

Front end prescription: Restrictive prescription authority is used in the front-end or pre-prescription approach to stewardship. Except for a small number of clinicians, the use of several antibiotics is restricted and needs prior authorisation. Clinicians who do not have the right to prescribe the medicine in question must get permission to order it from the authorised antimicrobial steward. The benefit of the front-end strategy is that it targets certain antibiotics for specific reasons based on regional trends of resistance and hospital formularies [4].

Back end prescription: The post-prescription or back-end method of stewardship makes use of prospective review and feedback. Based on the available microbiology data and the clinical aspects of the case, the antimicrobial steward analyses current antibiotic orders and offers clinicians advice to continue, modify, change, or cease the medication [4].

Methods to minimise the usage of antibiotics in hospitals

Formulary Restriction: Every hospital has a formulary that restricts the drugs that are offered in order to encourage physicians to use those medications. Formulary restriction can be difficult for long-term acute care facilities that accept patients from multiple

acute care hospitals with different formularies because they may feel obligated to be able to provide the referring hospital with the same antibiotic resistance is less clear because a long-term beneficial impact on resistance has not been established, and in some cases, use may simply shift to an alternative agent with a resulting increase in resistance [5].

Clinical Recommendations: Recommendations can be based on national recommendations, but they should also take into account regional antimicrobial resistance trends and hospital-specific aims for lowering use. Education of healthcare professionals and feedback on antibiotic use and patient outcomes can help in the implementation of guidelines [5].

Pharmacist-Driven IV to Oral Switch Programs: The majority of practitioners are unable to recall which drugs will provide roughly the same blood level as the intravenous. For this reason, if a patient satisfies specific requirements, many hospitals allow pharmacists to write orders to move highly bioavailable antibiotics (and other drugs) from the intravenous to the oral formulation. When a patient is clinically stable, eating normally, and taking other oral prescriptions, the pharmacy will automatically switch them to oral medications to save money without endangering the patient [4].

Antibiotic cycle: In a given patient care unit, antibiotic cycling refers to the regular removal and replacement of particular antimicrobials or antimicrobial classes. The idea is to regularly discontinue using particular types of antibiotics in order to prevent the emergence of resistance.

Antimicrobial order forms: These documents can help with the application of practice guidelines and be a useful part of antimicrobial stewardship [5].

Pharmacodynamics Dosage Optimization: Pharmacodynamics dose optimization is one stewardship strategy that is increasingly being adopted. The use of particular antimicrobials in previously unorthodox and frequently off-label ways is guided by concepts like the pharmacodynamics parameter, which is correlated with efficacy and knowledge of achievable tissue concentrations.

Combination therapy: Insufficient evidence exists to support the routine application of combination therapy to stop the formation of resistance. Combination therapy does have a place in some clinical settings, such as empirical therapy for seriously ill patients at risk of contracting multidrug-resistant infections, to broaden the scope of coverage and improve the chances of receiving effective first treatment [4].

One of the three explanations listed below is frequently used to support the initial use of combination therapy for illnesses caused by Gram-negative bacteria:

Enlarge the empiric coverage offered by two antibacterial drugs with various activity spectra (an effort to ensure that the pathogen is adequately covered by/. at least one of the two components of the regimen)

To take advantage of the synergy that two antibiotic drugs exhibit in comparison to one when used in vitro (and hence improve clinical outcomes)

To stop or postpone the development of resistance when receiving antimicrobial therapy [6].

Audit and feedback: The medical infection specialist or a specialist pharmacist can manage the audit and feedback process for the prescriber. Specialist nurses or clinical pharmacists, however, can also be educated to support this procedure depending on the intervention.

Antibiotic "Time outs": In hospitalised patients, antibiotics are frequently started empirically while diagnostic data is being gathered. However, even if further clinical and laboratory data, such as culture results, become available, providers frequently do not reconsider their choice of antibiotic. When the clinical picture is more clear and there is more diagnostic data available, an antibiotic "time off" prompts a reevaluation of the counting requirement for antibiotic choice. 48 hours after starting antibiotics, all providers should reassess their antibiotic regimens [7].

Monitoring the use and resistance of antibiotics: Computer-based surveillance can help with good stewardship by allowing for more precise antimicrobial intervention targeting, following the antimicrobial resistance pattern, and spotting nosocomial infections and adverse drug reactions.

De-escalation or streamlining of therapy: De-escalation or streamlining of empirical antimicrobial therapy based on culture results and elimination of redundant combination therapy can more effectively target the etiological microorganisms, reducing antimicrobial exposure and significantly reducing cost. Because continuing too broadly promotes to the selection of organisms that are resistant to antibiotics, good stewardship to promote prudent usage may clash with good stewardship to optimise empirical initial antimicrobial therapy.

By providing patient-specific culture and susceptibility data to optimise individual antimicrobial management and by assisting infection control efforts in the surveillance of resistant organisms and in the molecular epidemiologic investigation of outbreaks, the clinical microbiology laboratory plays a crucial role in antimicrobial stewardship [5].

Educational Activity: Since antimicrobial stewardship is a multi-disciplinary programme, every healthcare provider's contribution to the establishment of a successful ASP in the hospital is crucial. Therefore, encouraging the best use of antimicrobial agents is one of the pharmacist's duties for antimicrobial stewardship and infection prevention and control [8].

METHOD

In a tertiary care hospital, this prospective observational study was conducted. In a predetermined data collection form, the patient's demographic and medically pertinent information was gathered. However, these case charts were examined. The prescription and case charts were examined using the prescription guidelines, tertiary sources, Micromedex, Medscape Lexicomp, and reference materials. The patient's demographic information was kept private and further examined in accordance with the hospital's antibiotic policy. The necessary information regarding the patients who were prescribed antibiotics was noted down during the ward rounds and pre-rounds with consultants and residents. Later, the hospital's computer system was used to cross-check the culture/sensitivity reports. The information was gathered from the doctor's notes and progress charts, which are conveniently located at the patient's bedside, in the event that the ward rounds were missed. Review and documentation of the medication records of the patients admitted to the ward were done using pre-designed data collection forms. Demographic information, a current diagnosis, medical history,

prescribed medications (dosage, route, therapy duration, and indication), marketing categories (generic/brand, single/fixed-dose combinations), a lab study, and presenting complaints are all included in the data collection. It also includes information about when empirical therapy began, the date samples were collected for cultures and sensitivity tests, the organism that was isolated, the specimen that was obtained, sensitive and resistant antibiotics, changes in antibiotic therapy, restricted antibiotics, adverse drug reactions, and an assessment of compliance with the hospital's antibiotic policy. Until the day of discharge, the patients' conditions are continuously monitored while being further assessed for infection improvement. The findings have been recorded and thoroughly reported. The data was compiled in an excel sheet, then after being further analysed using the right statistical techniques.

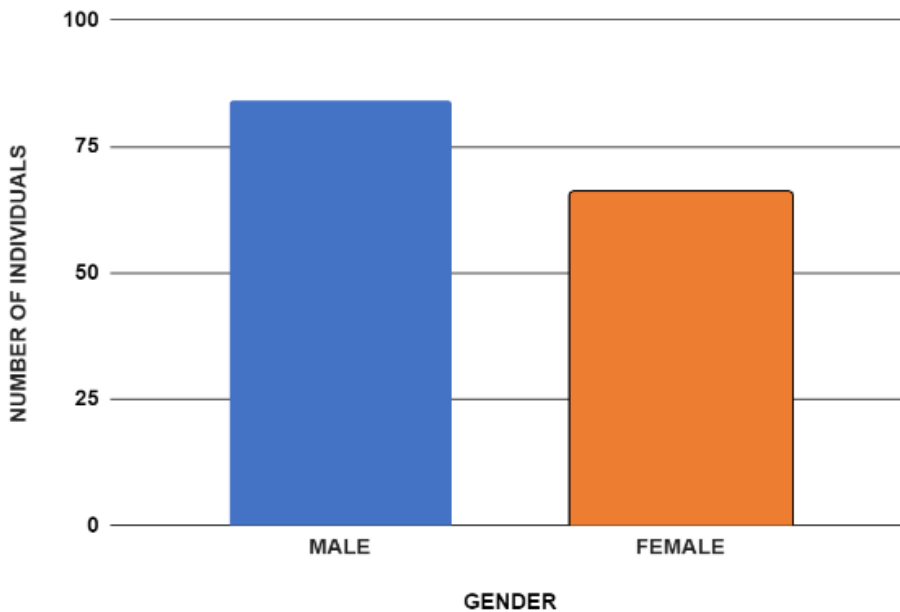
Ethical considerations:

Privacy and confidentiality of the research participants will be protected.

Result:

Fig 1. Gender distribution of inpatients

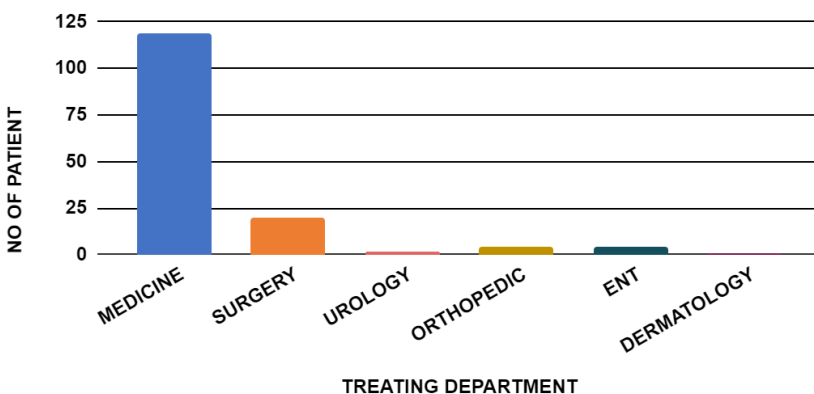
NUMBER OF INDIVIDUALS



In the gender distribution of the study population, 84(56%) patients of the total population were found to be male and 66(44%) patients were females respectively.

Fig2. Distribution of the study population by various treating department

DISTRIBUTION OF STUDY POPULATION BY VARIOUS TREATING DEPARTMENT



Out of 150 patients registered for the study, 119 (79.33%) were admitted in the medicine ward, 20 (13.33%) patients in the surgery ward, 4 (2.66%) patients in orthopaedic & ENT department. Urology department 2 (1.33%) & 1(0.66%) of patients in the dermatology department.

Fig 3. Frequency of various diagnosis in the study population

FREQUENCY OF VARIOUS DIAGNOSIS IN THE STUDY POPULATION

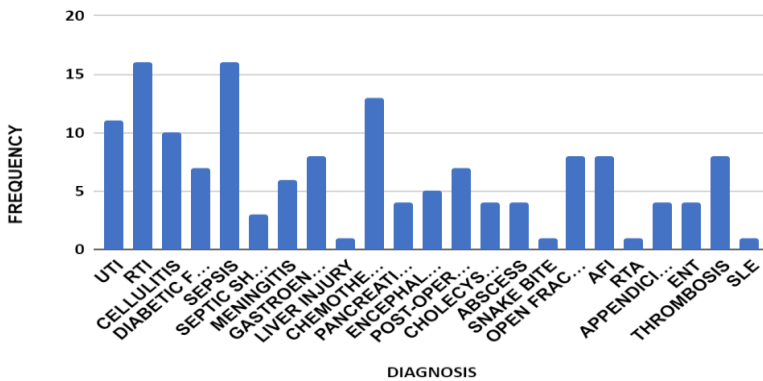
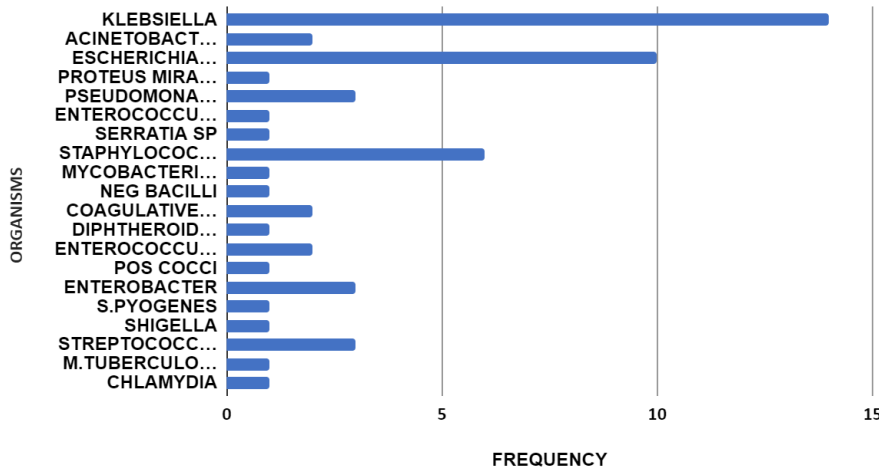


Fig 4. Various organisms found in the c/s test & their frequency.

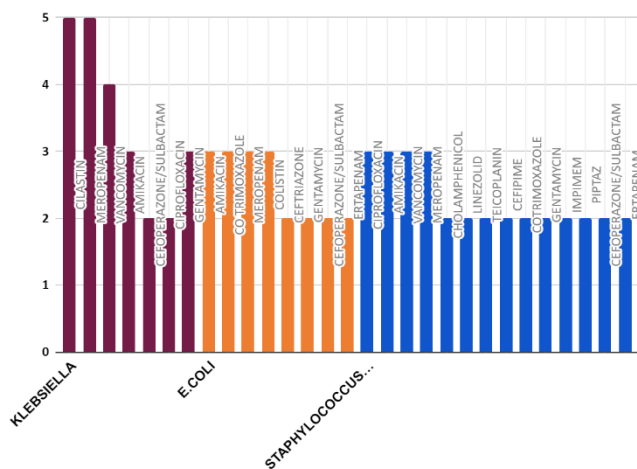
VARIOUS ORGANISMS IN C/S TEST & THEIR FREQUENCY



Among the culture tests obtained klebsiella was most frequently observed 14 (25%), followed by E coli 10 (17.85%), & staphylococcus aureus 6 (10.71%) and other organisms less frequent entries.

Fig 5. Sensitive antibiotic to frequently occurring organism in C/S test.

FREQUENT ORGANISM & THEIR SENSITIVE ANTIBIOTIC



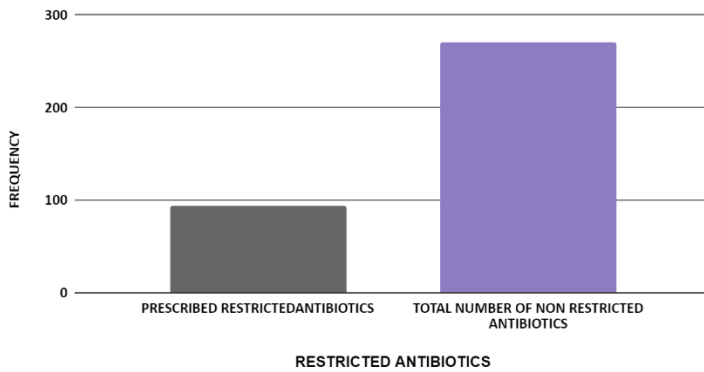
The klebsiella, E. coli & staphylococcus aureus are the most frequently observed organisms in C/S test. The most sensitive antibiotics towards klebsiella are cilastin & meropenam. Whereas for E coli it is amikacin, co-trimoxazole, meropenam & colistin. Ciprofloxacin, amikacin, vancomycin & meropenam are most sensitive to Staphylococcus aureus. These findings are based on the average of occurrence observed in the study population.

RESTRICTED ANTIBIOTICS

Antimicrobial resistance (AMR) leads to increased morbidity, mortality, and healthcare expenditure. The rate of development of AMR is accelerated by the use and misuse of antimicrobials. Preauthorization and restricted use of high-end antibiotics are the key modalities of antimicrobial stewardship. Hence, choosing the right antibiotics is the key to better clinical outcomes and preventing resistance in hospitals as well as communities. Here in out

Fig 6. Total count of prescribed antibiotic and other antibiotics

TOTAL COUNT OF PRESCRIBED RESTRICTED ANTIBIOTICS WITH OTHER ANTIBIOTICS



Restricted antibiotics prescribed were found to be 94 (30.22%) of the total antibiotics 311.

Table 1. Various restricted antibiotics in the prescription and their frequency

| RESTRICTED ANTIBIOTIC | FREQUENCY | PERCENTAGE % |
|-----------------------|-----------|--------------|
| MEROPENEM | 26 | 27.65% |
| COLISTIN | 11 | 11.70% |
| AMIKACIN | 1 | 1.06% |
| LINEZOLID | 5 | 5.31% |
| IMIPENEM & CILASTATIN | 3 | 3.19% |
| TIGECYCLINE | 2 | 2.12% |
| VANCOMYCIN | 1 | 1.06% |
| TEICOPLANIN | 1 | 1.06% |
| PIPTAZ | 44 | 46.80% |
| TOTAL | 94 | 100 |

Table 2. Common bacterial diagnosis where restricted antibiotics were used.

| BACTERIAL DIAGNOSIS | NUMBER OF RESTRICTED ANTIBIOTICS | PERCENTAGE |
|------------------------------|----------------------------------|------------|
| RESPIRATORY TRACT INFECTIONS | 4 | 11.70% |
| URINARY TRACT INFECTIONS | 3 | 8.82% |
| SEPSIS | 27 | 79.41% |
| TOTAL | 34 | 100% |

Restricted antibiotics were used the most in sepsis patients 27(79.41%) may be in order to avoid end organ damage or prevent septic shock followed by RTI & UTI.

Respiratory tract infection and urinary tract infection

Among 150 patients 16(10.6%) were found to have Respiratory tract infection (RTI). It is classified as upper respiratory tract infection and lower respiratory tract infection. LRTI has the highest prevalence in the inpatient hospital setting. Other comorbidities also add up to acquiring infection to an individual.

Among 150 patients included in the study population 11 (7.33%) were found to have Urinary Tract Infection. The most predominant isolate was klebsiella which was highly sensitive to linezolid and vancomycin. Followed by Escherichia coli highly sensitive to meropenem and Piperacillin/tazobactam.

Table 3. Frequency of RTI & UTI

| DISEASE | NUMBER OF INDIVIUALS | PERCENTAGE |
|---------|----------------------|------------|
| RTI | 16 | 10.6% |
| UTI | 11 | 7.3% |
| TOTAL | 150 | 100% |

Table 4. Drugs prescribed in RTI and their frequency

| DRUGS | FREQUENCY | PERCENTAGE |
|-----------------------------|-----------|------------|
| COLISTIN | 2 | 9.09% |
| AZITHROMYCIN | 2 | 9.09% |
| PIPERACILLIN AND TAZOBACTAM | 4 | 18.18% |
| AMOXICILLIN CLAVULANATE | 2 | 9.09% |
| MEROPENEM | 4 | 18.18% |
| CEFTRIAZONE | 4 | 18.18% |
| CEFUROXIME | 1 | 4.54% |
| DOXYCYCLINE | 1 | 4.54% |
| TEICOPLANIN | 1 | 4.54% |
| LINEZOLID | 1 | 4.54% |
| TOTAL | 22 | 100% |

Table 5. Drugs prescribed in UTI and their frequency

| DRUGS | FREQUENCY | PERCENTAGE |
|---------------------------|-----------|------------|
| PIPERACILLIN & TAZOBACTAM | 4 | 22.22% |
| MEROPENAM | 2 | 11.11% |
| CEFTRIAZONE | 4 | 22.22% |
| AZITHROYCIN | 2 | 11.11% |
| CEFOPERAZONE | 1 | 5.55% |
| COTRIMOXAZOLE | 1 | 5.55% |
| IMIPENAM & CILASTIN | 1 | 5.55% |
| COLISIN | 1 | 5.55% |
| MOXIFLOXACIN | 1 | 5.55% |
| TIGECYCLINE | 1 | 5.55% |
| LINEZOLID | 18 | 100% |

Discussion:

The objectives of antimicrobial stewardship programmes have been to ensure that antimicrobials are used appropriately to give the greatest patient outcomes, reduce the risk of side effects, increase cost-effectiveness, and lower or stabilise levels of resistance. However, there is still a lot of space for growth in terms of these goals' progress. Given its financial and personnel limitations, every hospital should make the best use of its available resources to assemble a successful team. A successful programme depends on effective communication and collaboration with the professionals in the hospital epidemiology, microbiology laboratory, and administration. These relationships can also be beneficial when the programme is implemented in a hospital context. Because it offers the Framework necessary to improve the sensible use of antibiotics, stewardship is especially important in the inpatient context of tertiary care hospitals.

Between January 2021 and June 2021, data on 150 patients who were diagnosed with a bacterial infection and admitted to the wards were examined. According to the demographic findings, 66 (44%) patients were female and 84 (56%) patients were determined to be men overall, with the majority of patients in the (46 to 70) year age range being admitted primarily to the medical ward. Similar to the study conducted by Meher BR, Mukherjee D et al. included 200 patients, of which 116 (58%) were men and 84 (48%) were females, with a mean patient age of 48.8 years [9].

In order to ascertain compliance with the antibiotic policy in the intensive care unit (ICU) of a tertiary care hospital, compliance with the recently introduced antibiotic policy was examined for a period of six months in both the current study and a prospective study conducted by Banerjee t, Anuprabha S, et al. In their study, 21.18% of participants complied with the antibiotic policy. While 105 (70%) patients were determined to be in accordance with the Bangalore Baptist Hospital's antibiotic policy, 28 (18.66%)

patients were found to be non-compliant. The old hospital policy, which failed to identify several disease conditions, was the cause of the noncompliance [10].

In a different surveillance study by Bergmans DC, Bonten MJ et al., they found that of all antibiotics prescribed for therapy, (49%) respiratory tract infection, (19%) abdominal infection, and (13%) sepsis were the three most common infections. They also noted the incidence of infections, antibiotic use, and antimicrobial susceptibilities of pathogen supply. In the currently conducted study, it was discovered that respiratory tract infection 4 (11.70%), urinary tract infection 3 (8.82%), and sepsis 6 (7.60%) are the most frequent bacterial diagnoses where the restricted antibiotic is administered. More than 40% of all admissions to inpatient hospitals were due to these infections. Therefore, preventing respiratory tract infections in their environment is probably the most efficient way to lower the need for antibiotics. Even while RTI may not be as widespread as an epidemic in this study, it is unquestionably the most often diagnosed bacterial infection. Therefore, preventing RTI can drastically cut down on the need for antibiotics [11].

Urinary tract infections were the most prevalent infections (54.9%), according to a study by Pattanayak C, Patnaik S, et al. in Odisha, Eastern India's Hitech Medical College and Hospital. *E. coli* (52.7%), *P. mirabilis* (15.4%), and *Ps. aeruginosa* (13.2%) were the two most common isolates. *E. coli* had high levels of resistance to cephalexin, cefadroxil, tobramycin, and prulifloxacin while being very susceptible to polymyxin B, gatifloxacin, and ceftriaxone. Similar to this, a recent study at Bangalore Baptist Hospital found that *Klebsiella* 14 (25%) was the most frequent bacterial infection in inpatient hospitals. *E. coli* 10 (17.8%) and *Staphylococcus aureus* species 6 (10.71%) are the two most prevalent bacteria that cause infections. *Pseudomonas aeruginosa*, *Enterobacter* sp., and *Streptococcus pneumoniae* were also often found in 3 (5.3%). In contrast, other species, such as *Acinetobacter* species, *Coagulative negative staphylococcus*, and *enterococcus* sp., were found in 2 (3.5%) each. As opposed to this, only one of each of the following species was present: *Proteus mirabilis*, *S. pyogenes*, *Shigella*, *M. tuberculosis* and *chlamydia*, *Enterococcus faecalis*, *Serratia* sp, *Mycobacterium*, *Neg bacilli*, *Diphtheroid Bacilli*, and *Pos Cocci* [12].

Respiratory tract infection (RTI) was shown to be the most frequent infection in Sheth K. V., Patel TK, et al retrospective review of the indoor case papers. For Gram-negative isolates (GNIs), imipenem and meropenem were the most effective antibiotics, whereas vancomycin was the most effective antibiotic for Gram-positive isolates (GPIs). The current study's efforts have shed light on the most popular medications for treating common medical conditions. Treatments for urinary tract infections that are more successful include piperacillin/Tazobactam, meropenem, colistin, and linezolid [13].

Conclusion:

According to the gender breakdown of the study population, 66 (44%) patients were female and 84 (56%) patients were male, with the majority of patients in the (46 to 70) year age range—71 (47.33%)—admitted mostly to the medical ward.

Respiratory tract infections 4 (11.70%), urinary tract infections 3 (8.02%), and sepsis 27 (79.41%) are the most frequent bacterial illnesses for which limited antibiotics are prescribed. More than 40% of all admissions to inpatient hospitals were due to these infections. Therefore, reducing the use of limited antibiotics can help reduce antibiotic resistance by causing less exposure and minimising the spread of serious infectious diseases in the population.

With a total of 44 (46.80%) prescriptions, piperacillin/tazobactam is the most often prescribed restricted antibiotic found in the inpatient prescription. The doctor uses this medication in both empirical and definitive therapy.

The following is a list of some of the antibacterial elements on which the study has concentrated:

Patients who followed Bangalore Baptist Hospital's antibiotic policy made up 105 (70%) of the total population, while 28 (18.66%) patients did not. The obsolete hospital policy, in which numerous medical conditions weren't addressed, as well as the lack of patient reports on culture and sensitivity were the causes of non-compliance.

Finally, this study's efforts have shed light on the most popular medications for treating common medical conditions. For respiratory tract infections, doctors often prescribe Piperacillin with Tazobactam, Meropenam, and Ceftriaxone. Similar to how linezolid, ceftriaxone, meropenem, and piperacillin/tazobactam are more successful in treating urinary tract infections.

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