A Prospective Observational Study on Prescribing Patterns of Restricted Antimicrobials and Determining Outcomes

1R. Srinidhi, 2Mohd. Athar Hussain, 3Simhadri Sugnaneswary, 4G. Sushmitha, 5A. V. Kishore Babu

1,2,3Doctor of Pharmacy Intern, 4 Asst. Professor and of college, 5Professor and Head of Department
Department of pharmacy practice,
Bhaskar Pharmacy College, Bhaskar Nagar,
Yenkapally (V), Moinabad (M) Hyderabad, Telangana, India-500075.

Abstract-
Background: Treatment with Antimicrobial agents appears to be so efficacious and rational that they are occasionally prescribed for dubious indications and for extended than required where the priority for adverse effects and development of resistance is hardly any. AMR could be a global problem. Eradication of AMR requires a big reduction within the use of antimicrobials. As a result, some antimicrobials are restricted and prescribed only under the supervision of a physician for which they are grouped under Restricted Antimicrobial Agents.

Objective: This study illustrates the factors influencing the need for prescribing Restricted Antimicrobials and evaluating the patient outcomes. Restricted Antimicrobials are regularly classified under a ‘traffic light system’. While this isn't a necessary need, one of these machines is diagnosed throughout many Australian healthcare centers and it's far usually taken into consideration to be an effective device for teaching prescribers approximately a local policy of restricted antimicrobials.

Methodology: The study was conducted over a period of 6 months at territory hospital. A total of 114 patients were considered. This study was conducted on those patients who got admitted in general wards.

Results: Study carried out in those subjects revealed that most of the cases were of CAI and had got admitted due to LRTI (18%) followed by surgery (17%) and the highly prescribed RA was found to be Meropenem (41%). Patients who got specific therapy got less no. of hospital stay. Samples were collected from subjects for culture tests before starting therapy and was found that most of the organisms detected to be KLEBSILLA (23.4%) and E. COLI (10.6%) and maximum no. Of organisms detected were found to be resistant to Ciprofloxacin (13.2%) and Levofloxacin (10.6%). Outcome showed that 89% of the patients got successfully treated and discharged.

Conclusion: AMS can offer all healthcare professionals an intention to save the public from an inappropriate use of AMR and help in achieving positive outcomes in patients. In our study, we observed that patients receiving specific therapy benefited more than patients on empirical therapy and surgical prophylaxis. Through our study, we conclude that RA has greater impact in treating various infections and decreasing resistance.

Keywords: Antimicrobials, Resistance, Restricted Antimicrobials, Global problem, Positive outcomes, Successful therapy.

INTRODUCTION:
The factor that rubs out microscopic life forms or ceases their expansion (1). Antimicrobial drug treatments may be sorted in step with the microscopic living entities that behave themselves mostly conversely, as an illustration, bacterial growth is destructed by antibiotics, and against fungal growth, antifungals are prescribed. They can also be graded according to their functioning. Improvements in antimicrobial technology have led to answers which could move past genuinely hindering microbial boom. Rather, positive forms of porous media were advanced to assassinate microorganisms (2). To fight communicable disorders, antimicrobial drugs which might be powerful in controlling, eradicating, or getting rid of the boom of beasts of prey of microbes has been advanced. The highest of those antimicrobial drugs present in herbal merchandise in which they had been at first utilized by diverse creatures to shield against an attack of microbes (3,4). Had in fact been remote and marked, a lot of those “herbal” merchandise was in the end changed through humanity to propose extra or magnified action of antimicrobials (3). The moves of a lot of those antimicrobial drugs are precise to precise kinds of infectious organisms even though others may also have an effect on vast tiers of microorganisms. The management of antimicrobial agents within the remedy and eradication of communicable disorders has aggravated an evolitional reaction amongst microorganisms through generating antimicrobial resistance (5). The main causes of AMR are microbial, human, clinical usage, public perception and behavior, vaccination reluctance.
The execution of suitable formulary regulations of antimicrobial drugs is taken into consideration a center method of antimicrobial stewardship in Australian hospitals (6). This Recommended list of Antimicrobial Restrictions presents steering to centers that might

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be enforcing restricted antimicrobial and accepting rules, with its content material primarily based totally on each current list and professional thought. The listing presents facts on which antimicrobial drugs are typically restricted, the maximum typically endorsed quantity or stage of limit and justifies the standards for the limit of every agent. The rationale for Restrictions for Antimicrobials: The instance for enforcing antimicrobial regulations inside a medical institution formulary could be very well developed (9).

Restriction types are of 2 types, Expert Approval and Criteria-based. Restrictive standards are decided through a panel that checks antimicrobial stewardship and/or the Drug and Therapeutics Committee. Criteria-based regulations are beneficial for enhancing the effectiveness of prescribing antimicrobials, however, at instances can be difficult to screen and impose.

Restriction levels Restricted Antimicrobials are regularly classified under a ‘traffic light system’. While this isn't a necessary need, one of these machines is diagnosed throughout many Australian healthcare centers and it's far usually taken into consideration to be an effective device for teaching prescribers approximately a local policy of restricted antimicrobials. RED - Highly Restricted. They need opinions from an infectious disease (ID) doctor or scientific microbiologist (or a nominated scientific officer) earlier to apply, but a few limits can be criteria-based in which these are effective. Deliberations have to receive on a way to manipulate pleas for extraordinarily confined antimicrobials in risk and/or pressing conditions 24 hours a day, 7 days a week.

ORANGE - Restricted Orange drugs are regularly issued to criteria-based regulations. Many orange antimicrobials are confined to apply for decided-on indicators or for a restrained quantity of time (e.g., 24 to seventy-two hours) previous to searching for consent from an ID doctor or scientific microbiologist, or a nominated scientific officer. These markers regularly need consent after starting therapy. Some markers can be labeled orange for precise indicators and red for all different indicators.

GREEN - Unrestricted Green antimicrobial drugs ought to be prescribed reasonably and effectively, however, don't have any precise regulations on their utilization.

Details of Restriction: Information on Restriction must be decided and revised through the council that checks antimicrobial stewardship and must be able to reflect on nearby assets and requirements. Prescribers, pharmacists, and different scientific workforce need to have geared up to get the right of entry to complete restricted lists in each department. Restriction information must be saved clean and brief and might split up antimicrobial drugs primarily based totally on dosage form products and direction of management wherein effective.

A Cochrane assessment of interventions to enhance antibiotic prescribing for health facility inpatients categorized those techniques into 3 most important business names: persuasive interventions: those consist of education, audit and feedback, suggestions, and scientific pathways. Restrictive interventions: formulary restriction, previous approval or preauthorization from infectious diseases (ID) health practitioner, microbiologist or pharmacists, automated forestall orders, antimicrobial biking or scheduled switch, antibiotic order forms. Structural interventions: automated records, automated choice support, instance CPOE (8).

Few restricted antimicrobials used in a Tertiary Care Hospital are as follows: Meropenem, Teicoplanin, Tigecycline, Posaconazole, Polymyxin-B, Cilane, Colistin, Ertapenem, Doripenem, Aztreonam, Vancomycin, Caspofungin, Linezolid, Anidulafungin, Voriconazole, Amphotericin-B, Fosfomycin, Micafungin.

MATERIALS AND METHODS:
- **Study site:** Territory hospital (Yashoda Hospitals, Secunderabad.)
- **Study design:** Prospective observational study.
- **Study period:** 6 months from the day of approval (October 2021- March 2022)
- **Study population:** 114 Subjects
- **Study criteria:**
  - Inclusive criteria:
    Ø Patient who are conscious and cooperative and who are willing to give informed consent
    Ø All patients who are being prescribed by Restricted Antimicrobials irrespective of age, gender, diagnosis, lab and culture tests
    Ø Patients who are on both oral and parenteral route of administration of prescribed Restricted Antimicrobials.
    Ø Patients who expired during the course of study or those who got discharged even before he got completely cured
    Ø Post covid patient
    Ø Patients who have undergone surgery shifted to general wards are included
  - Exclusive criteria:
    Ø Patients who are not willing to give consent forms
    Ø Covid patients
    Ø Patients who are in ICU’s
    Ø HIV patients
    Ø Pregnant and lactating mothers
- **Sources of data collection:** All relevant and necessary data was collected from:
  Ø Patient case notes
  Ø Treatment charts
  Ø Laboratory reports
  Ø Consulting nurse or physician about the patient
  Ø Any other significant source
- **STUDY DESIGN:** The data collecting form, which was designed to collect, document, analyze data includes following details:
  Ø Patient demographic details
  Ø Chief complaints
Ø Diagnosis
Ø Past illness
Ø Present illness
Ø Previous medication history
Ø Comorbidities
Ø Present medication history
Ø Lab investigations
Ø Culture results
Ø Reason for prescribing
Ø Place where infection occurred

Ø Tools:
Ø Data collection form
Ø Any surgical prophylactic form
Ø Restricted Antimicrobial lists
Ø Standard antimicrobial guidelines
Ø Hospital antimicrobial guidelines

- **Study procedure:**
Ø Should visit the respective general wards regularly
Ø Those patients listed in inclusion criteria were selected for conducting study
Ø All appropriate data from the case sheets and any other sources were collected
Ø Should be properly designed and documented
Ø Collected data was analyzed using suitable methods

- **Methodology:** About 114 subjects in total with different diagnoses attending the in-patient department (IPD) were involved in the study. Before the start of study, permission from the hospital authorities was obtained and also the informed consent form from the subjects was obtained. Through the data collection form involving patient demographic details, past and present history, comorbidities, diagnosis, previous medications sufficient and required data was collected and follow ups were done till the patient was discharged.

**RESULTS:**
In these 6 months study, total of about 114 patients prescribed with Restricted Antimicrobials were evaluated,

- **Based on diagnosis:**
Out of 114 patients, Majority of patients diagnosed with lower respiratory tract infection (18%) are prescribed with Restricted Antimicrobials followed by surgical prophylaxis (17%)

![DIAGNOSIS](image-url)
➢ **Based on restricted antimicrobial administration:**

Among the subjects for whom Restricted Antimicrobials was prescribed, majority of the patients received meropenem i.e., 41%, followed by linezolid 16%.

![Figure II](image)

FIGURE II

➢ **Based on organisms found:**

Out of 114 patients whose samples were given for culture tests, the results shows that majority of the organisms i.e., 23.4% found was Klebsiella pneumonia, followed by E. coli (19.6%).

![Organisms Found](image)

FIGURE III

➢ **Based on resistant drugs:**
Among the subjects whose culture tests were conducted, majority of them (13.1%) showed resistance to ciprofloxacin, followed by levofloxacin (10.6%).

**FIGURE IV**

- **Based on reason for use:**
  Out of 114 patients, 54 patients (48%) were prescribed specifically i.e., after thorough culture tests were done, 46 patients (40%) were prescribed empirically, 8 patients (7%) were prescribed based on diagnosis and 6 patients (5%) were prescribed for surgical prophylaxis.

**FIGURE V**

- **Based on average of days of stay in hospital:**
  Among the subjects who had received specific therapy, were found to get discharged within 7 days after their admission in the hospital whereas patients who received therapy based on diagnosis had longer hospital stay.
➢ **Based on patient outcomes:**
Out of 114 patients, majority of the patients i.e., 89% of the patients were discharged successfully.

![Average of days of stay in hospital](image)

**FIGURE VI**

**FIGURE VII**

**DISCUSSION:**
1) All the organizations consisting of the health care sectors should implement policies which direct the health professionals to follow rational drug use so that they help in minimizing most of the resistance by antimicrobials (9).
2) One such program is AMS (Anti-Microbial Stewardship) which includes policy of prescribing Restricted Antimicrobials under the approval of Infectious committee
3) In this prospective study, we analyzed the reasons for prescribing restricted antimicrobials. In our research, our survey exhibits that a higher group of subjects (18%) diagnosed with Lower respiratory tract infections were prescribed with Restricted antimicrobials. In aid of this survey, the investigation by Sasima Kusuma Na Ayuthya et.al, shows that patients diagnosed with LRTI's need immediate therapy for those who were in critical condition along with medical practice by physician who have already gone through the difficulty in treating MDR organisms.
4) In our investigation, our results show that the maximum prescribed restricted antimicrobial was meropenem (41%). In support to this study, the research study by Jayalakshmi et.al reveals that patients who were admitted in other hospitals previously were prescribed by low end antibiotics which may develop resistance leaving the current hospital authorities with no choice of prescribing high end restricted antibiotics mainly meropenem.
5) In our study, the study found to be more rapid in patients receiving specific therapy (48%) than in empirical (40%) and surgical prophylaxis (5%). According to previous investigations conducted by apaticha pungiitrapapij et.al suggests the importance of following the hospital’s antibiotic formulary to avoid inappropriate antibiotic use. In their study, it reveals that inappropriate antibiotics were prescribed to 42% of patients (empirical therapy), 82% of patients (surgical prophylaxis) and 39% of patients (based on diagnosis).
6) In our analysis, before initiation of prescribing restricted antimicrobials, culture tests were done for majority of patients (and also gram staining) to find out organisms and resistance to those drugs they are developing. It was found that, Klebsiella pneumonia (23.4%) and E. coli (19.6%) was found in higher percentages and most of the organisms are developing resistance against fluoroquinolones (ciprofloxacin-13.1% and levofloxacin-10.6%)
7) In the research inquiry by Demssi Ayalew Anttenah et.al, the exploitations made illustrated that only the lab investigations do not give conclusion about the infection and organism responsible for infection. This is obtained only through culture tests, thus widely helps in providing appropriate therapy against appropriate organism and reduce resistance. Based on the results, there will be a change from empirical to specific therapy based on requirements.
8) According to the research conducted by patricia tarcea biza et.al, 4 organisms namely pseudomonas aeruginosa, E. Coli, Acinetobacter and K. Pneumoniae are the main reason for most of the infections. Thus, they revealed that carbapenems are the primary choice prescribed as empirical therapy against infections caused by gram negative organisms.
9) In the study investigated by M. Thuong et.al, the study which was conducted to prove the adequate number of prescriptions for 4 antimicrobials found that fluoroquinolones were found to be inadequate. It is because fluoroquinolones were extensively utilized as a result of broad-spectrum activity and ease in availability in oral forms thus leading to non-medical adherence and developing resistance.
10) In our analysis, patients who received specific therapy were discharged within a week or we can conclude that length of hospital stay was less when compared to patients who received empirical therapy and surgical prophylaxis. In support to this statement, the study conducted by patricia tarcea biza et.al, the patients who are on empirical therapy need to go through the de-escalation therapy which provide many benefits to patients.
11) In the study conducted by shiv Kumar et.al suggests that antimicrobials for normal infections should be prescribed for minimum for 3–5 days and sometimes it may prolong more than a week or 2 based on the patient's condition.
12) In our research, the most common reason for patients in admitting the hospital is the community acquired infections (83%). In contrast to this study, the evaluation made by Kumar DK et. Al suggests that the main aspect of prescribing restricted antimicrobial is that long length of hospital stay, and hospital acquired infections. Their studies also revealed that utilization was more in hospital acquired infections than in community acquired infections. Thus, AMS program plays a vital role in reducing the unnecessary use of antimicrobials.
13) In accordance with our study, the study conducted by M. Thuong et.al suggests that the most inappropriate therapy prescribed for community acquired infections for which narrow spectrum antimicrobials must have been used.

CONCLUSION:
Today resistance to antimicrobials is posing a greater threat to the universe. It is because patients are showing not much response to drugs against dreadful infections because of resistance developing against many antimicrobials. So, our main aim is to decrease resistance. Antimicrobial stewardship can offer all healthcare professionals an intention to save you from the inappropriate use of antimicrobials that causes resistance and help in achieving positive outcomes in patients. Through our study, we conclude that restricted antimicrobials have a greater impact in treating various infectious diseases and decreasing resistance. The main parameters required for the need of prescribing such antimicrobials can be obtained through specific therapy where culture tests were done by drawing samples from patients. The benefit obtained from this specific therapy is that based on the culture reports, we can find out the organisms that are responsible for infections and to what drugs it is susceptible and resistant. As per the reports, effective therapy is obtained. It should be kept in mind that there are certain regulations or guidelines to be followed before prescribing any restricted antimicrobial. The recovery rate is found to be more rapid in patients receiving specific therapy than empirical therapy and surgical prophylaxis. It is because through cultures physicians are able to prescribe the appropriate restricted drugs. Usually, empirical therapy should be followed for not more than 3 days and if patients show no recovery, then they are switched to specific therapy by sending culture to find out the exact reason whether the prescribed drug is susceptible or not, as a result, length of hospital increases. One drawback of prescribing empirical therapy is that more resistance might be developed because the therapy is based on lab investigations and physicians' experience. It is because lab investigations may vary from patient to patient and if prescribed drugs are found to be resistant then there is a chance for the recommendation of de-escalation therapy. In surgical prophylaxis, it is necessary to prescribe most of the restricted antimicrobials based on hospital guidelines in order to prevent infections that usually
get infected after surgery. There are some other factors through which based on patient's demographics like age, gender, BMI, and comorbid conditions these restricted antimicrobials are prescribed. Thus, AMS implementation gives us more benefits. Unfortunately, in India, these programs are now developing and still, many hospital authorities are unaware of them. It is a duty of a clinical pharmacist to educate people and health professionals about such programs in order to decrease resistance and make them understand that antimicrobial stewardship should be a part of our day-by-day practice, we will enhance affected person protection and care, lessen the needless use of precious assets, and decrease.

**Abbreviations:**

**REFERENCES:**