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A study on physician compliance with antibiotic De-Escalation practices and implementation of antimicrobial stewardship programmes in a tertiary care hospital

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Abstract

Introduction: De-escalation of empirical antibiotic therapy is an essential part of antimicrobial stewardship programmes. It involves streamlining antibiotics to lower broad-spectrum antibiotic exposure based on microbiological cultures. This leads to effective targeting of the causative pathogen and at the same time, reduce the development of resistant microorganisms. As antibiotic-resistant microorganisms have become a clinical challenge in both inpatient and outpatient settings, such practices are increasingly employed in healthcare settings.

Aim: The study aims to promote and measure the use of an appropriate agent, dose, duration, and route of administration of antimicrobial agents in order to improve patient outcomes while minimizing adverse events, including toxicity.

Methods: A prospective observational study was conducted in a tertiary care hospital. The sample size was 500 patients. The study was performed from October 2019 to September 2020. The participant's details were collected from patient medical records. The data obtained was analysed with MS Excel and the study results were expressed in number and percentages.

Results and Discussion: The number of blood samples and cultures obtained during the study period was noted. In our study, the percentage of single antibiotic prescriptions was highest in July 2020 (68.75%) as compared to other months while multiple antibiotic prescriptions were highest in January 2020 (82.75%). The number of antibiotics continued after obtaining the culture report was highest in February (30) while the highest percentage was seen in August 2020 (89.65%). The percentage appropriate de-escalation was highest in the month of April (82.35%) while September saw the highest number of multiple antibiotic prescriptions (25).

Conclusion: The present study revealed positive results towards antibiotic de-escalating practices in the clinical settings to improve patient outcomes and reduce the use of antimicrobials which, in turn, can contribute to slowing down the further development of antibiotic resistance in hospitals.

Keywords: antibiotic resistance, antibiotic de-escalating practices, microorganism, antimicrobial stewardship

Introduction

The field of medicine underwent a revolutionary change after the discovery of penicillin-the first antibiotic-in the late 1920s. Subsequent development and introduction of newer classes of antimicrobials led to remarkable improvements in health outcomes. Diseases with high mortality such as tuberculosis were no longer considered fatal. However, overuse of these anti-infectious agents has caused the emergence of resistant strains of microorganisms–ones that could send us back to the pre-antibiotic era.

The number of antibiotics introduced in the market has decreased considerably over the course of time. Simultaneously, there has been a monumental increase in the number of drug resistant microorganisms reported with incidences of resistance even among new, high end antibiotics such as ceftazidime-avibactam [1].

This is a serious cause of concern which is why the WHO considers antimicrobial resistance (AMR) to be a part of the top 10 serious global health threats [2]. The Review on Antimicrobial Resistance has estimated that AMR is responsible for causing 700,000 deaths annually [3]. Furthermore, the Independent O'Neill Review predicts these numbers to rise to 10 million by 2050-a death toll higher than what both diabetes and cancer contribute together today [4].

The incorrect prescribing of antibiotics can contribute to drug resistance among microorganisms. In the US, inappropriate prescribing was seen in 30-50% of the cases [5]. In addition, another study found that antimicrobial use deviated from the recommended guidelines in 55.9% of the cases treated against community acquired pneumonia and urinary tract infections [6].

Similar reports have reviewed the relationship between inappropriate use of antimicrobials in an acute care setting to increasing number of resistant pathogens resulting in a significant impact on patients' morbidity, mortality, and increasing health care costs.

In Australia, over 30 million prescriptions of antibiotics had been dispensed in 2014 with nearly half the population receiving at least one course of treatment [7]. This overuse prompted authorities to implement the golden rules of antimicrobial prescribing-the 'MINDME' guidelines [8]. The Australian Therapeutic Guidelines recommend prescribers to follow these rules while prescribing antibiotics.

Table 1: The features of MINDME guidelines

Golden Rules of Antimicrobial Prescribing "MINDME":	
M	Microbiology guides therapy wherever possible
I	Indications should be evidence based
N	Narrowest spectrum required
D	Dosage appropriate to the site and type of infection
M	Minimise duration of therapy
E	Ensure monotherapy in most cases

India-the largest consumer of antibiotics in the world-is rife with antimicrobial misuse. A study conducted by the University of Washington found that the use of antibiotics increased-despite authorities warning against misuse-especially during the first peak of the COVID-19 pandemic [9]. The study concluded that policy changes are required and that antimicrobial stewardship programmes are the need of the hour.

Antimicrobial stewardship programmes combat AMR by promoting the rational use of antimicrobials. The WHO defines antimicrobial stewardship (AMS) to be a coherent set of actions which promote the responsible use of antimicrobials at individual, national, and global levels, and across human health, animal health, and the environment [10].

Antimicrobial stewardship is, there fore, an inter-professional effort across the continuum of care and includes [11].

- Timely and optimal selection, dose, and duration of an antimicrobial
- Ensuring the best clinical outcome during treatment or prevention of infection, with minimal toxicity to the patient
- Having minimal impact on resistance and other ecological adverse events such as C. difficile

The WHO defines an antimicrobial stewardship programme (AMS programme) to be an organizational or system-wide health-care strategy to promote the appropriate use of antimicrobials through implementation of evidence-based interventions [10]. Studies regarding AMS programmes have been positive in terms of cost-effectiveness and reduced consumption of antibiotics [12, 13, 14]. As successful as AMS programmes have been, antibiotic-resistant microorganisms have become a clinical challenge in both inpatient and outpatient settings. A recent systematic review on the effectiveness of antimicrobial stewardship programmes against bacterial resistance has concluded that there is no solid evidence of AMS programmes being effective against resistant bacteria in the hospital care settings [15]. Hence why, it is essential to conduct more number of scientifically sound studies in the hospital care settings to provide conclusive proof that AMS programmes are truly effective against drug resistance.

AMS programmes require inter-disciplinary effort from all healthcare professionals-doctors, nurses, pharmacists-to ensure its proper implementation. There is huge scope for pharmacists as they are experts in handling medications, including antibiotics. Timely, appropriate interventions can be life-saving and improve therapeutic outcomes in severe infections.

A convenient but important strategy employed in antibiotic stewardship programmes is antibiotic de-escalation. It involves discontinuing or replacing a broad spectrum antibiotic with a narrow spectrum one with hopes of decreasing antimicrobial use and improving patient outcomes. Therefore, antimicrobial de-escalation has 2 major features: the intention to narrow antimicrobial coverage based on subjective and objective evidence, and the commitment to stop antimicrobial treatment if infection is not established [16]. Furthermore, a third feature that a single antibiotic rather than multiple ones should be use wherever possible was also added [17].

A review article on antimicrobial de-escalation found many advantages to this method which include [18]:

- Minimal changes in treatment outcomes when compared with the conventional approach
- Beneficial impact on the antimicrobial resistance profile at the micro and macro level for the institution
- Decreased incidence of antibiotic related adverse events
- Reduction in the cost of antimicrobial therapy

The same review also suggests that by day 3 of treatment in sepsis patients, decisions ought to be made whether to stop antibiotic therapy, continue it, escalate or de-escalate it based on pathogens identified, sensitivity results and clinical progress of the patients. These decisions should be reviewed upon each assessment of the patient.

The awareness on de-escalation practices in antimicrobial stewardship programmes is increasing and therefore, at a local level, we aim to assess the appropriateness of the antimicrobials prescribed in the hospital with specific focus on the effectiveness of the de-escalation practices carried out and the compliance of physicians in such practices.

The standards followed by the antimicrobial stewardship committee at our hospital are given in table.2.

Table 2: AMS programme measures followed at the hospital

GGHC AMS program measures for quality improvement	
Structural measures	**Process measures**
▪ Availability of multi-disciplinary antimicrobial stewardship team	▪ Compliance with acute empiric guidance (documented notes and policy compliance)
▪ Availability of guidelines for empiric treatment and surgical prophylaxis	▪ Percentage appropriate de-escalation; percentage appropriate switch from IV to oral
▪ Provision of education in the last 2 years	▪ Compliance with surgical prophylaxis (<60 minutes from incision, <24 hours and compliance with local policy)

Aim

To promote and measure the use of an appropriate agent, dose, duration, and route of administration of antimicrobial agents in order to improve patient outcomes while minimizing adverse events, including drug toxicity

Objectives

- To reduce infections with Gram-positive or Gram-negative resistant bacteria
- To reduce surgical infection rates
- To minimize unintended consequences of antimicrobial usage
- To educate prescribers, pharmacists, and nurses about good antimicrobial prescribing practices and antimicrobial resistance
- To streamline the use of antimicrobials during the rounds

Methods

Study type: Prospective observational study
Inclusion criteria: All patients with positive blood cultures
Exclusion criteria

- Blood culture contaminants
- All other positive urine, swab, pus culture are excluded from study

Data collection period: The data was collected from October 2019 to September 2020

Data sources

- Patient records
- Microbiology lab

Results

Our study noted the number of blood samples collected and the corresponding number of positive blood cultures obtained which have been graphically presented. It can be seen that the highest number of samples and positive blood cultures were collected in the month of August (29 samples and 44 blood cultures) followed by 36 samples collected and 39 blood cultures turning positive in February. In November, the lowest number of samples and cultures (14 each) were obtained.

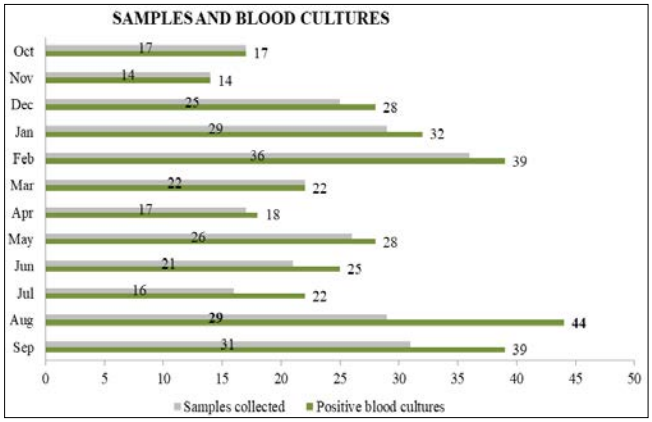

Fig 1: Blood samples and cultures collected during the course of study

We also calculated the numbers and percentages of single and multiple antibiotic prescriptions in the hospital. The numbers are given in the table while the percentages are presented in the graph.

Table 3: Single and multiple antibiotic prescriptions in numbers

Month	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept
Single	5	8	10	5	11	9	6	9	12	11	10	11
Multiple	12	6	15	24	25	12	11	17	9	5	19	19

The number of multiple antibiotic prescriptions is more than the single prescriptions in each month, except November, June and July. The highest number of multiple antibiotic prescriptions can be seen in the month of February (25) while single antibiotic prescriptions are the highestin June (12 in number). The percentages were calculated and it can be seen that July (68.75%) had the highest percentage of single antibiotic prescriptions while January had the lowest (17.24%). The opposite pattern is seen for multiple antibiotic prescriptions.

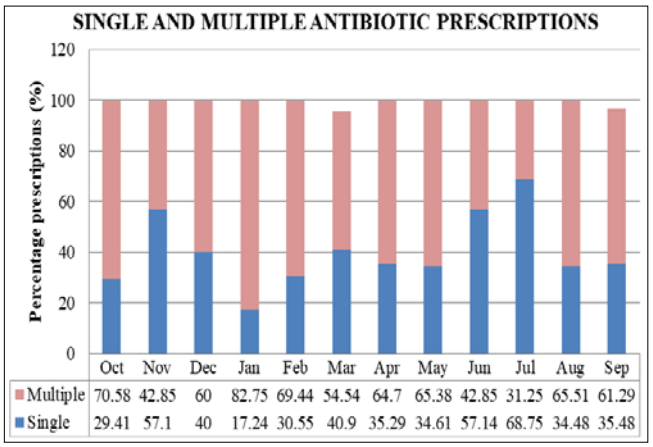

Fig 2: Percentages of single and multiple antibiotic prescriptions

Our study has also identified the numbers and percentages of antibiotics continued after the results of the culture report were obtained. The number of antibiotics continued and the percentages are given in table. and fig…, respectively.

Table 4: Number of antibiotics continued after culture report

Month	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sept
Antibiotics continued	8	5	13	17	30	13	10	17	12	8	26	20

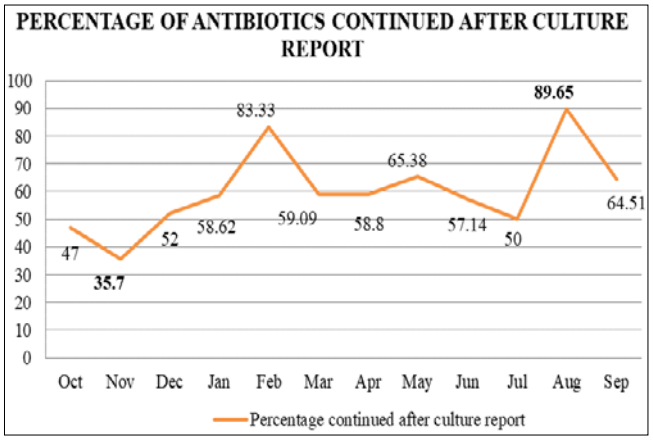

Fig 3: Percentage of antibiotics continued after culture report

It can be seen that although the highest number of antibiotics continued after the culture report was in February (30), the highest percentage is attributed to the month of August (89.65%) whereas the lowest, in terms of both numbers and percentage, is observed in the month of November (5, 35.7%).

Through our results, it can be seen that the initial empirical therapy with antibiotics started by physicians before obtaining culture reports was very appropriate.

Lastly, we calculated the percentage of appropriate de-escalation. It can be seen that the highest percentage of de-escalation was carried out in April with 82.35% followed by June and September with 80.95% and 80.64%, respectively. The lowest can be seen in the month of November with 50%. September (25) saw the highest number of multiple antibiotic prescriptions while November had the least number of it (7).

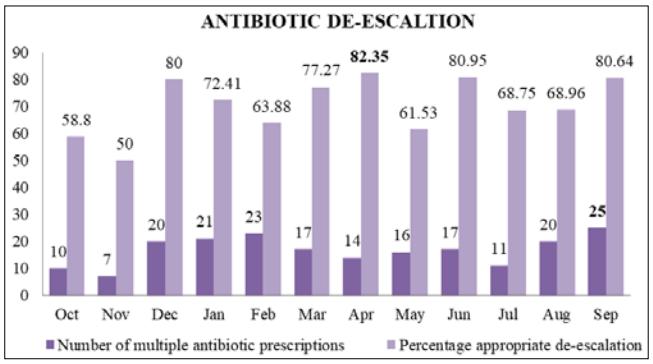

Fig 4: Percentage appropriate de-escalation of antibiotics performed during the study

The de-escalation of the initial antimicrobial regimen was performed in 219 patients (35%). The hospital mortality rate was 27% in patients with de-escalation, while with those with no treatment change and escalation, it was found to be 33% and 43%, respectively (P=0.006). De-escalation therapy was a protective factor (OR 0.54; 95% CI 0.33-0.89).

Inadequate empirical antimicrobial therapy (Odds-Ratio (OR) 0.58; 95% confidence interval (CI) 0.36-0.93).

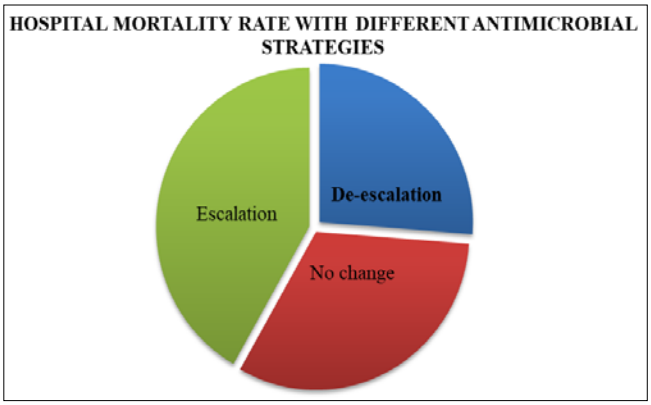

Fig 5: Distribution of hospital mortality rates with different antimicrobial strategies

Discussion

Most studies with antibiotic de-escalation have been performed in patients with pneumonia where de-escalation was beneficial in reducing mortality, shorter ICU stay and overall hospital stay, provided the treatment was appropriate [18, 19]. Antibiotic de-escalation has also been found to be beneficial in healthcare settings other than the ICU such as the emergency medicine wards though further studies are required to confirm this [22].

Among patients with sepsis, de-escalation therapy of antimicrobials has been associated with lower mortality than with no change in treatment and escalation of antibiotics. In the same study, 35% of the cases underwent antibiotic de-escalation [23]. A similar study involving patients with nosocomial sepsis, de-escalation was performed in 43% of the cases, concluding that it can be performed in less than 50% of the patients in such a highly focused environment such as the intensive care unit [20].

The number of blood samples drawn and the positive cultures obtained in our study was much higher, especially in the last two months of the study. We have also observed that multiple antibiotics have been more commonly prescribed to patients than single antibiotics. This can be attributed to many reasons such as the severity of the disease, the pathogen identified, the condition of the patient, to name a few.

We have also noted the number of antibiotics continued after the receipt of the culture report. The percentages have been estimated based on the number of samples collected during the corresponding month. We have observed a pattern that greater the number of samples obtained, greater was the number of antibiotics continued.

Finally, we calculated the percentage appropriate de-escalation. We found that the minimal percentage was 50% with the maximum being 82.35%. Therefore, we can establish that antibiotic de-escalation practices are being followed at the hospital in an appropriate manner. It is also important to note that well established antimicrobial stewardship programmes are necessary to properly incorporate antibiotic de-escalation as it is not standardised and many barriers exist that hinder its application [21].

More research is required to study the compliance of physicians with de-escalation practices in developing countries. A study assessing physician compliance with antibiotic de-escalation in Jordan found that doctors were poorly compliant with these practices. The authors, through their study, stressed the need to execute antibiotic de-escalation in the intensive care unit [24]. To the best of our knowledge, our study, which is similar to the one above, is also one of the first of its kind to investigate physician compliance with antibiotic de-escalation in patient care areas. Through our data, it can be seen that there is a positive attitude of physicians in implementing antibiotic de-escalation where desirable.

Majority of our respondents also agreed that clinical pharmacists have a prominent role in undertaking the responsibility of implementing the AMS programme more effectively in healthcare settings. A study conducted in South India identified that clinical pharmacists have been imperative in improving compliance with AMS and anti-tubercular therapy recommendations implicating that their involvement is crucial in implementing and sustaining AMS programmes [25]. Therefore, the contributions and interventions of clinical pharmacists would greatly benefit the de-escalation process-a key feature of AMS programmes-in hospitals, especially the multi-speciality ones.

Conclusion

Infectious diseases have been in existence from time immemorial. They are very common in both developed and developing countries all across the globe. The misuse of antimicrobials has led to the development of antimicrobial resistance which is why de-escalation practices of antimicrobials have been employed in hospitals. Since it is an important component of antimicrobial stewardship programmes, its use will allow easier integration of such programmes in hospitals in order to ensure that antimicrobials will not be dispensed without a valid prescription. Co-operation between different healthcare professionals is essential to ensure successful implementation of AMS programmes. Our study results have identified that the empirical antimicrobial therapy initiated by physicians was very appropriate. Though our study has shown positive results towards antibiotic de-escalation and the attitude of physicians toward such practices in the clinical settings, more studies are required to

investigate the effectiveness of clinical pharmacist interventions in hospitals to improve the standards followed in hospitals and to lower the rates of antimicrobial resistance. Some of the intervention performed by them include: stopping antibiotics with negative culture reports-prevents antimicrobial resistance due to reduced exposure of antibiotic-after 10 days, modifying antimicrobial therapy (dose increase, decrease, change or stoppage of antibiotic) based on the liver and renal function tests of the patient.

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