

Study on Implementation of Antibiotic Stewardship Program
at Apollo Hospital, Chennai

By

Reshma Ramesh

*Dissertation submitted in partial fulfillment of the requirements of the degree
MBA Hospital and Health Management*

Academic year, 2017-2019



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TO WHOM SO EVER IT MAY CONCERN

This is to certify that Ms. Reshma Ramesh student of MBA Hospital and Health Management from The IIHMR University, Jaipur has undergone internship training at Apollo Hospitals, Chennai from 04th Feb 2019 to 4th May 2019.

The candidate has successfully carried out the study designated to her during the internship training and her approach to the study has been sincere, scientific and analytical.

The Internship is in fulfilment of the course requirements.

I wish her all success in all her future endeavors.

A handwritten signature in blue ink, appearing to read 'Ashok'.

Dr. Ashok Kaushik

Dean, Academics and Student Affairs

The IIHMR University, Jaipur

16 May 2019

A handwritten signature in blue ink, appearing to read 'Nutan'.

Dr. Nutan P Jain

Professor

The IIHMR University, Jaipur

07th May 2019

To Whom So Ever It May Concern

This is to certify that Ms. Reshma Ramesh, a student of IIHMR University, Jaipur has completed her internship successfully in the Department of Quality System Office at Apollo Hospitals, Chennai from 04th February 2019 to 04th May 2019.

During her internship, she has displayed her commitment, hard work and passion to learn and assist others. I wish her all the best for all her future endeavours.

Warm Regards



S V Kiran

Vice President - Human Resources

Southern Region & Karnataka Region

THE IIHMR UNIVERSITY, JAIPUR

CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled A study on the implementation of Antibiotic Stewardship Program at Apollo Hospitals, Chennai submitted by Ms. Reshma Ramesh IIHMR-U/01/2017-19/0646 under the supervision of Dr. Nutan P. Jain for award of MBA in Hospital and Health Management in Health and Hospitals of the University carried out during the period from 4th Feb 2019 to 4th May 2019 embodies my original work and has not formed the basis for the award of any degree, diploma associate ship, fellowship, titles in this or any other institute or other similar institution of higher learning.



Signature

RESHMA RAMESH.

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A STUDY ON IMPLEMENTATION OF ANTIBIOTIC STEWARDSHIP PROGRAM AT APOLLO HOSPITALS, CHENNAI

ABSTRACT

BACKGROUND:

There has been an increased emergence of antibiotic resistant micro-organisms and the consequence of this resistance has led to increased morbidity, mortality and cost of care to the patient. Infections are the most common reasons for patients to seek medical advice and for antibiotics to be prescribed. Inappropriate or indiscriminate use of antibiotics can increase the cost of care by increasing drug cost, increasing toxicity, increasing resistance, and increasing laboratory costs. A good prevention and control programme requires administrative and scientific leadership and a financial and human resource commitment.

OBJECTIVES:

The objectives of the study were: (1) To review the antimicrobial stewardship program at Apollo Hospital, Chennai, and (2) To analyse the appropriateness of Antibiotic Stewardship Program using input, process and output measures.

METHODOLOGY:

The study is descriptive in nature. Antimicrobial Stewardship Program policies and guidelines were reviewed, and the process was mapped. A total 515 patients who received High-End Antibiotics – Meropenem, Poly B, Colistin and Tigecycline in the Critical Care Unit, Specialty ICU and Wards during February to May 2019. The analysis was conducted using Systems Framework- Input, process and outcome. Cost reduction analysis was also conducted.

RESULTS:

Antibiotic Stewardship Program is a hospital-based program, initiated to improve the optimum use of antibiotics, to optimise the treatment of infections, to reduce the adverse events of antibiotic use, to reduce the multi drug resistant organisms and to reduce the cost of care to the patients. Out of 515 total patients, 145 patients were under definitive therapy and 370 patients were empiric therapy. Of 370, 344 patients who received empiric therapy were eligible for de-escalation. The percentage of de-escalation was found to be around

93%. The cost saved by a patient who received empiric therapy on an average was found to be INR 33,000.

CONCLUSION:

A strong infection prevention and control program and successful antimicrobial stewardship efforts can have reducing Multi-Drug Resistant Organisms. The Antibiotic Stewardship Program was found to be effective by measuring its input, process and output measures.

GLOSSARY :

ASP	Antibiotic Stewardship Program
DE	De-escalation
Poly B	Polymyxin B
CCU	Critical Care Unit
ICU	Intensive Care Unit
MDRO	Multi-Drug Resistant Organism
HAI	Hospital Acquired Infection
ICN	Infection Control Nurse
O.T	Operation Theatre
ID	Infectious Disease
GPC	Gram Positive Cover
GNB	Gram Negative Cover

INTRODUCTION:

There has been an increased emergence of antibiotic resistant micro-organisms and the consequence of this resistance are increased morbidity, mortality and cost of care to the patient. The main aim of the Antibiotic stewardship Program is to control the over use of broad-spectrum antibiotics which can reduce the multi drug resistant organisms (MDRO). A strong infection prevention and control program (IPC) and successful antimicrobial stewardship efforts can have reducing MDROs. A good Prevention and Control programme requires administrative and scientific leadership and a financial and human resource commitment. [1]. Hence the best partner for Anti-microbial Stewardship for an organisation is its Prevention and Control of Infection. It assesses the burden and ensures the incidence of Hospital Acquired Infection (HAI) rates are low. This is done by formulating policies, educate the health care professionals, the visitors about infection prevention strategies, monitor adherence, investigate outbreaks of HAI's, and prepare organizations for new infectious threats, like MDROs or pandemic influenza. These practises can synergize with those of an ASP to help reduce the burden.

Antibiotic overuse and misuse are one of the main reasons that have led the bacteria to mutate strain to evade the killing action of the drugs. For example, the *Clostridium difficile* normally colonises in the colon of the human large intestine, most of the drugs are inactive, instead the drugs destroy the normal flora of the gastrointestinal tract and allowing the spore-forming pathogen to promulgate. [2]

Anti-microbial resistance patterns can vary regionally and even among different hospitals within the same community. Infections are the most common reasons for patients to seek medical advice and for antibiotics to be prescribed. Inappropriate or indiscriminate use of antibiotics can increase the cost of care by increasing drug cost, increasing toxicity, increasing resistance, and increasing laboratory costs. Prophylactic antibiotic use in some hospitals remains a problem. Antibiotics are prescribed unnecessarily and empirically for complaints where no antibiotic is required or where culture and sensitivity results could be safely awaited.

The purpose of this study is to analyse the antibiotic usage pattern between four high end antibiotics (Meropenem, Poly-B, Tigecycline and Colistin), the percentage of appropriate

de-escalation and the cost that is saved by de-escalation of high-end Antibiotics. These indicators help to measure the appropriateness of Antimicrobial Stewardship program.

OPERATIONAL DEFINITIONS:

- De-escalation: Discontinuing the high-end antibiotic or reducing to lower generation antibiotics in accordance to the culture sensitivity report.
- Empirical therapy: Initiating broad spectrum antibiotics when culture report is not available.
- Definitive therapy: Change in treatment of antibiotics according to the antimicrobial sensitivity pattern.
- High End Antibiotics: The organization has identified 10 high end antibiotics which are administered during septic shock and suspected multi drug resistance infection.

REVIEW OF LITERATURE:

- Cristina, L., Vincenza D., Giancarlo C., et all (2017). ‘A cost analysis of a broad-spectrum antibiotic therapy in the empirical treatment of health care-associated infections in cirrhotic patients.’

The study briefs about the use of broad-spectrum antibiotics which has resulted in cost-saving in Hospital Acquired Infection in Liver Cirrhotic patients. A retrospect data on antibiotic daily doses, days of treatment, length of hospital stay, and DRG (diagnosis-related group) was analysed and the profitability of hospitalizations was calculated by considering DRG tariffs divided by length of hospital stay. It was found that the profitability of hospitalisation with standard therapy was higher than broad spectrum therapy, but treatment failure was less with broad spectrum antibiotics.

- Ibrahim, E. H., Sherman, G., Ward, S., Fraser, V. J., &Kollef, M. H. (2000). ‘The Influence of Inadequate Antimicrobial Treatment of Bloodstream Infections on Patient Outcomes in the ICU Setting.’

The study was conducted to identify the patients who received inadequate antimicrobial treatment and arrive at a relationship between inadequate treatment and patient’s outcome. Less than half of the study population received inadequate antimicrobial treatment. The

mortality rate was high in patients who received inadequate antimicrobial treatment that group which received adequate antimicrobial treatment. This also gives rise to the fact that antimicrobial drug resistance can lead to septic shock and mortality.

- Mave, V., et al (2017). 'High Burden of Antimicrobial Resistance and Mortality Among Adults and Children with Community-Onset Bacterial Infections in India.'

In this article, the author describes the use of antibiotics has been repandly increased in the last twenty years. The study was conducted in a public hospital in Maharashtra, India provesthat there is a relationship between prior antimicrobial use and multi drug resistance micro-organisms and increased risk of mortality. The findings of the study suggest the prescription of empiric antibiotics in the community must be regulated. There is also a lack of data on the adverse consequence of MDR bacterial infection in low- and middle-income countries.

- Jan-Willem, H. et al (2016). 'Measuring the impact of antimicrobial stewardship programs.'

Jan-Willem says that the introduction of Anti-microbial stewardship program (ASP) involves all the stakeholders in the healthcare who have the necessary competence who can treat the infectious disease and tackle antimicrobial resistance. During the transfer of patients (internal and external) there is high possibility of spread of pathogens. Implementing the ASP can increase the probability of correct provisional diagnosis thus reducing the antimicrobial resistance, better treatment outcome and minimise the risk of toxicity to the patients.

- Marc, H., Maureen K., Michael, P., Gary, A., Noskin, Todd, A., Lee. (2009)
'Cost-effectiveness analysis of an antimicrobial stewardship team on bloodstream infections: a probabilistic analysis.'

The author measured the cost effectiveness in terms of QALY (quality adjusted life years) gained over life years. The antibiotic stewardship program is a multi- disciplinary set up which have efficient personnel to combat issues on antimicrobial resistance, right choice of antibiotics, preparation of antibiograms. Cost effective analysis is a measure to assess the interventions introduced. The incremental cost-effective ratio is calculated in blood stream infection treatment between standard treatment and ASP treatment. The study setting was

for a period of one year in ICU and non-ICU areas. It was found that the cost for continuing the ASP is in favour that the treatment will be cost effective to the hospitals who receive active therapy in blood stream infection.

RESEARCH QUESTIONS:

- 1) What is the antimicrobial stewardship program at Apollo Hospital, Chennai?
- 2) How is the antimicrobial stewardship program implemented at Apollo Hospital, Chennai?

OBJECTIVES:

- 1) To review the antimicrobial stewardship program at Apollo Hospital, Chennai.
- 2) To study the appropriateness of Antibiotic Stewardship Program using input ,process and output measures.

METHODOLOGY:

The study is descriptive in nature. The duration of the study was from February to May 2019. The study population includes all patients who received High-End Antibiotics – Meropenem, Poly B ,Colistin and Tigecycline in the Critical Care Unit, Specialty ICU and Wards. Expired patients and patients who left against medical advice , patients who received antibiotics as surgical prophylaxis and patients who received other broad and narrow spectrum antibiotics were excluded from the study. Stakeholders who are involved in the Antibiotic Stewardship Program I.e. Primary Consultant, Intensivists, Antibiotic Surveillance Nurse, CCU nurses, Infection Disease Consultants.

Methods of Data collection:

The ASP was reviewed and data from the patients records was collected. Information on patient name, UHID, diagnosis, antibiotic administered, duration, dosage were collected from patient file and from the antibiotic surveillance nurse .The cost for the vials of the antibiotics were collected from the pharmacy department.

Interaction with staff was done for better understanding of the workflow. Interaction was done with the following staff.

- *Clinical Pharmacist -1*
- *Primary Consultant-6*
- *Intensivists-3*
- *Antibiotic Surveillance Nurse- 1*
- *CCU nurses-2*
- *Infection Disease Consultants -3*

Data Collection Tools

Review and interactions were made based on Systems Framework- Input, process and outcome framework

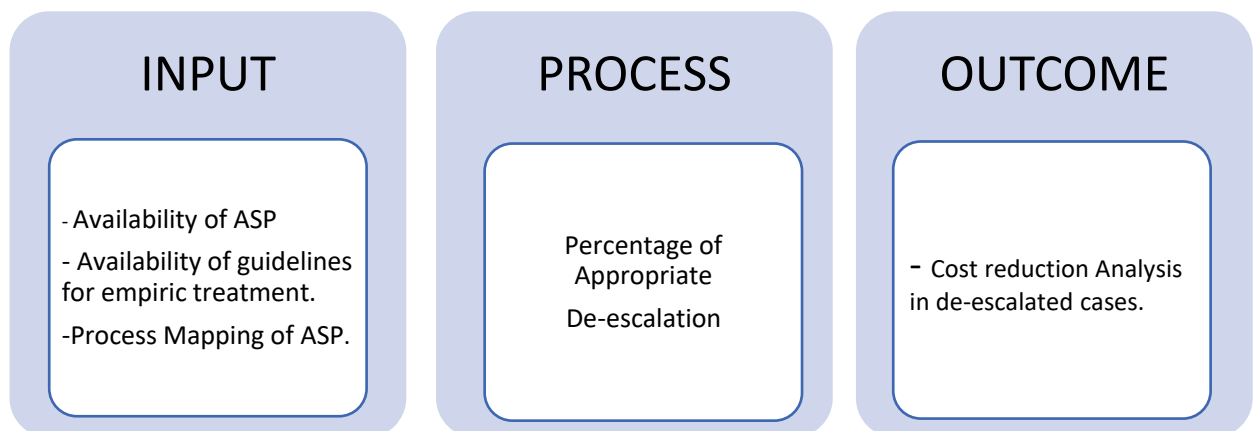
Data Analysis: A Process Flow was done based on the roles defined for each healthcare personnel. Cost reduction analysis was done using cost of the vials of Colistin, Poly-B, Tigecycline, Meropenem which was collected from the Pharmacy Department.

SYSTEMS FRAMEWORK ON ANTIBIOTIC STEWARDSHIP PROGRAM

The appropriateness of ASP was measured by input process and output measures.

[Fig:6.1 Systems framework on Input process and output of ASP.](#)

The table explains the indicators of the input, process and output which measures the appropriateness of Antibiotic Stewardship Program.



REVIEW OF ASP POLICIES AT APOLLO HOSPITALS,CHENNAI:

- A good Prevention and Control programme requires administrative and scientific leadership and a financial and human resource commitment.
- Aim of the Antibiotic stewardship Program is to control the over use of broad-spectrum antibiotics.
- Antibiotic Stewardship Program (ASP) is a hospital-based program, initiated
 - To improve the optimum use of antibiotics,
 - To optimise the treatment of infections and
 - To reduce the adverse events of antibiotic use.
 - To reduce the multi drug resistant organisms (MDRO).
 - And to reduce the cost of care to the patients.
- Helps the clinician to improve the quality of patient care and patient safety through improved cure rates, reduced treatment failures and increased frequency of correct prescribing of antibiotics for therapy and prophylaxis.

1.INPUT :

The ASP policies and guidelines were reviewed. Input measure of the ASP can be measured by the following

- **Availability of Antibiotic Stewardship Program.**

The Antibiotic Stewardship Program was first introduced in Apollo Hospitals, Chennai in 2009 with the aim,

- To improve the optimum use of antibiotics,
- To reduce the adverse events of antibiotic use.
- To reduce the MDRO
- and to reduce the cost of care to the patients.

This program helps the clinician to improve the quality of patient care and patient safety through improved cure rates, reduced treatment failures and increased frequency of correct prescribing of antibiotics for therapy and prophylaxis.

For a program to function effectively and efficiently, it should have a multidisciplinary team who are skilled to manage and prevent Hospital acquired infection.

The Members of the Antibiotic Stewardship program are

1. Infectious Disease Consultant
2. ICN – In charge
3. ICN – Antibiotic Surveillance Nurse
4. Clinical Pharmacist
5. Clinical Microbiologist.

The Infectious Disease Consultant meets with the ICN -in charge and the Antibiotic Surveillance Nurse daily and discuss about the prognosis of the patient who are under the high-end Antibiotics. The clinical Pharmacist analyses the Definitive Daily Dose of various antibiotics. The Clinical Microbiologist The team formulates policies for optimum use of antibiotic use for therapeutic and prophylaxis.

Policies that support optimal antibiotic use

Document the dose, duration, and indication of the drug :

The dosage, frequency and indication of the drug must be specified for all antibiotic treatment regimen. This ensures the information is available for further use.

1. Develop and implement facility specific treatment recommendations

With the base guidelines at national and local susceptibilities and formulary options We can optimize antibiotic selection and duration, particularly for common indications for antibiotic use like community-acquired pneumonia, urinary tract infection, intra-abdominal infections, skin and soft tissue infections and surgical prophylaxis.

2. Availability of guidelines for empiric treatment.

The hospital has established a set guideline which includes the choice of antibiotics , the type of specimen identified for the underlying disease , the dosage and frequency of antibiotic.

Appropriate cultures should be sent before initiating or changing the parental antibiotics. This helps to track the status of infection prior to the treatment and ensure comparability in the patient's prognosis.

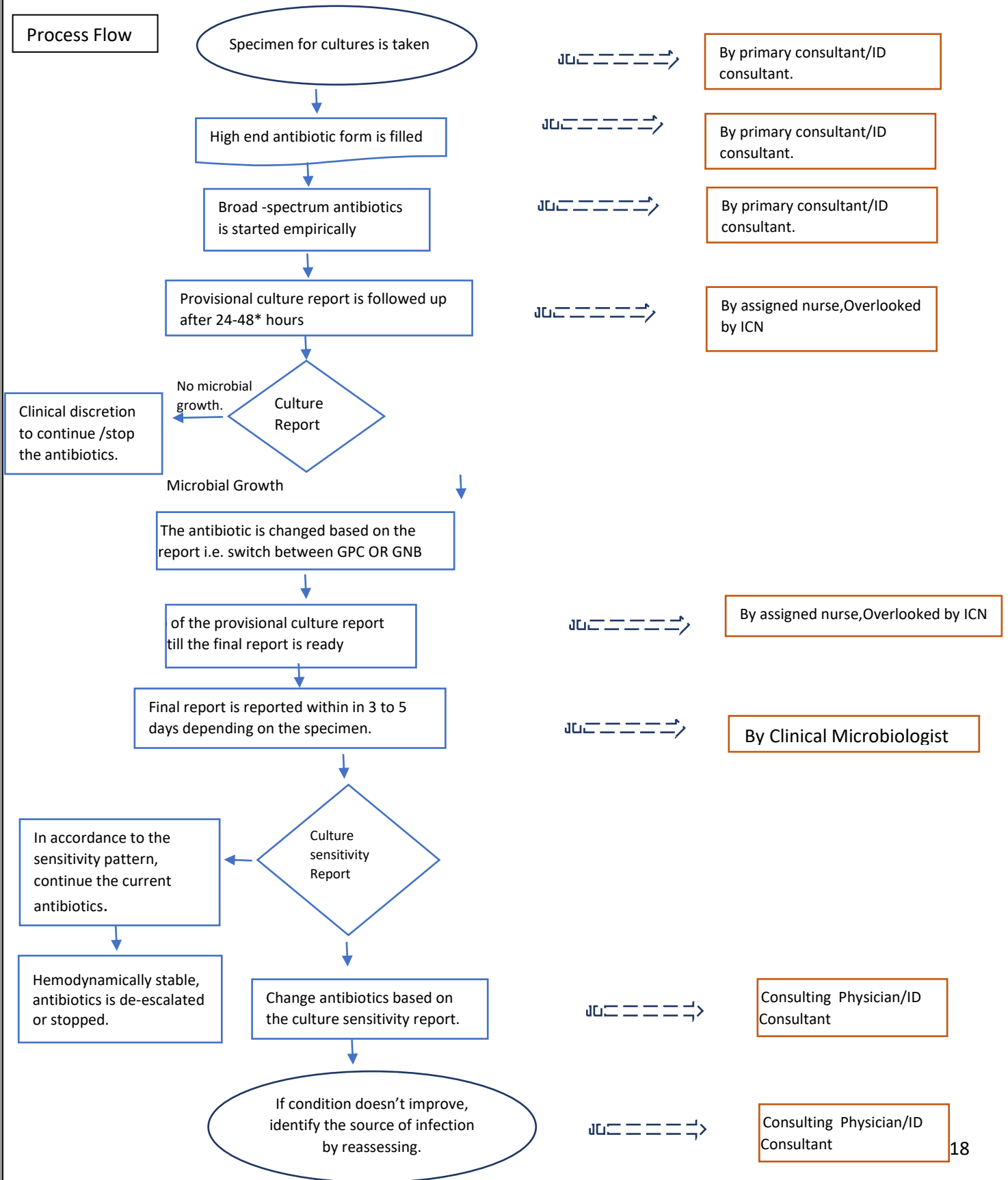
3. Process Mapping of Antibiotic Stewardship Program.

A standard process is followed on when and how the broad-spectrum antibiotic is de-escalated to narrow spectrum antibiotic. Each step of the process is well defined and designated to a healthcare personnel and can be traced.

Process Mapping for initiating high-end antibiotics in the treatment regiment

Personnel involved

Process Flow



2. Process :

The Appropriateness of ASP can be measured by calculation the percentage of appropriate de-escalation. There are various definition for De-escalation. According to the organisation, it has defined as discontinuing the broad-spectrum antibiotic to appropriate narrow spectrum antibiotic based on the culture sensitivity report. There are different means of de-escalation. It is strategy to decrease the emergence of resistance pattern , decrease in adverse drug reaction. However, there is no proven study which states de-escalation is safe for patients who are in septic shock which has a risk of re-infection .But studies have shown there is a shorter length of stay in patients who were de-escalated due to ASP than patients who received the standard therapy.

At Apollo hospital , de-escalation occurs at the following stages

1. When culture report showed no proven and the patient clinical status improves
2. When the patient clinical status improves after receiving a stat dose.
3. When a patient receives multiple antibiotics empirically and the number of antibiotics is reduced based on the culture report.

Fig. 6.2

When culture report shows microbial growth, and infectious consultant advises to de-escalate the antibiotics as per clinical discretion.

3. OUTPUT :

The outcome of appropriateness of Antibiotic stewardship Program can be measured by calculating the cost saved during appropriate de-escalation in empiric therapy. The organisation has defined guidelines which helps the physician to choose the right choice of antibiotic for specific disease condition. The guideline specifies the dosage and frequency of the antibiotics and the duration of the drug which must be administered. This is considered as the standard treatment regimen. To calculate the cost saved during de-escalation ,the total cost is subtracted from the anticipated cost.

DISCUSSION:

The percentage of appropriate de-escalation under empiric therapy was calculated. De-escalation can be done in empiric and definitive therapy. In this study, empiric de-escalation is taken into consideration since 71.8% of the total patients received empiric therapy remaining 29.2% of the population received definitive therapy.

Calculating the percentage of appropriate de-escalation.

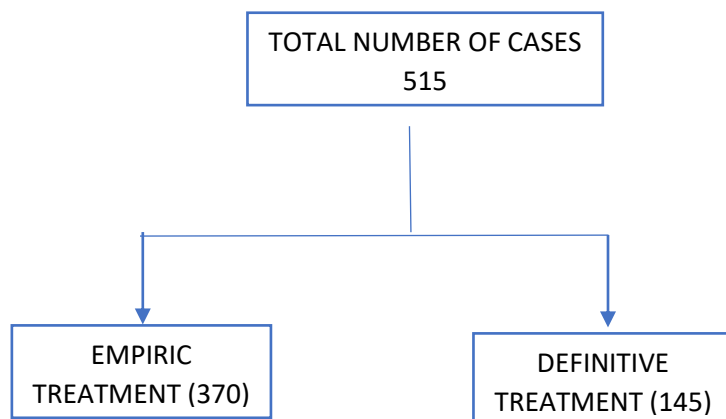


Fig 6.3: The above figure shows the total number of cases who received Meropenem, Poly B, Tigecycline and Colistin (515) out of which 370 received Empiric therapy and 145 received definitive therapy.

In this study, the patients expired due to severe sepsis, patients who left against medical advice and patients who received antibiotics as surgical prophylaxis have been excluded from the study. In such cases the patient is either too weak to withstand the antibiotic

therapy or in LAMA cases the prognosis of the treatment cannot be assessed. The consumption pattern of antibiotics between Meropenem, Poly B, Tigecycline and Colistin is given below.

DRUG	n
MEROPENEM	234
POLY B	45
COLISTIN	45
TIGECYCLINE	40
TOTAL	344

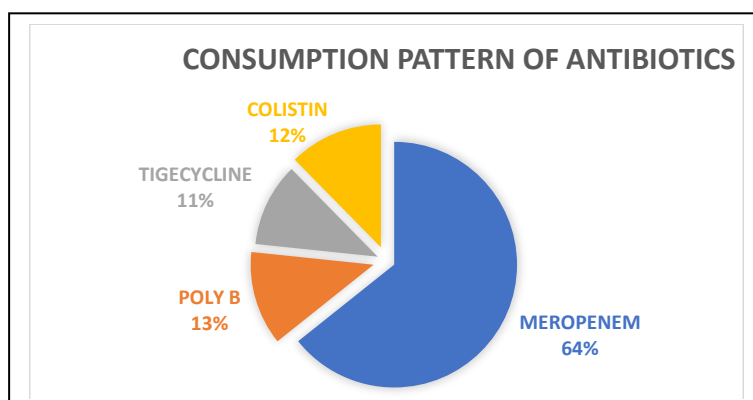


Fig 6.4: The above graph explains that Meropenem was the majority consumed antibiotics and tigecycline was consumed in minimum.

- Percentage of patients who are eligible for ASP intervention resulting in cost saving
= $370/515 = 71.8\%$
- Out of the 370 patients, 344 patients are eligible for de-escalation.
- Percentage of appropriate de-escalation in empiric therapy = $344/370 = 92.9\%$
- The remaining patients (N=26) continues as definitive therapy as de-escalation is not possible due to their co-morbid conditions.

The organisation has defined the criteria for de-escalation depending on the patient's clinical status, pathogenicity and the resistance of bacteria against the antibiotics.

S.NO	CRITERIA FOR DE-ESCALATION	N
1.	Culture report showed no proven and the patient clinical status improves.	17
2.	Patient clinical status improves after receiving a stat dose.	90
3.	Patient receives multiple antibiotics empirically and the number of antibiotics is reduced based on the culture report.	87
4.	Culture report shows microbial growth, and ID Consultant de-escalates the antibiotics as per clinical discretion.	150
	Total number of patients de-escalated	344
	Percentage of appropriate de-escalation = $(344/370) * 100$	92.9%

Fig 6.5: The above table explains the criteria for de-escalation and the number of cases which underwent de-escalation at various stages.

As the study population included all the wards , speciality ICU and CCU, they have patients from all specialites.Hence there is no discrimination among patients. Majority of the cases come under intra-abdominal infection (N=73) and skin -soft tissue infection (N= 60). There were minimum patients who were diagnosed with Hospital Acquired infection(N=9)

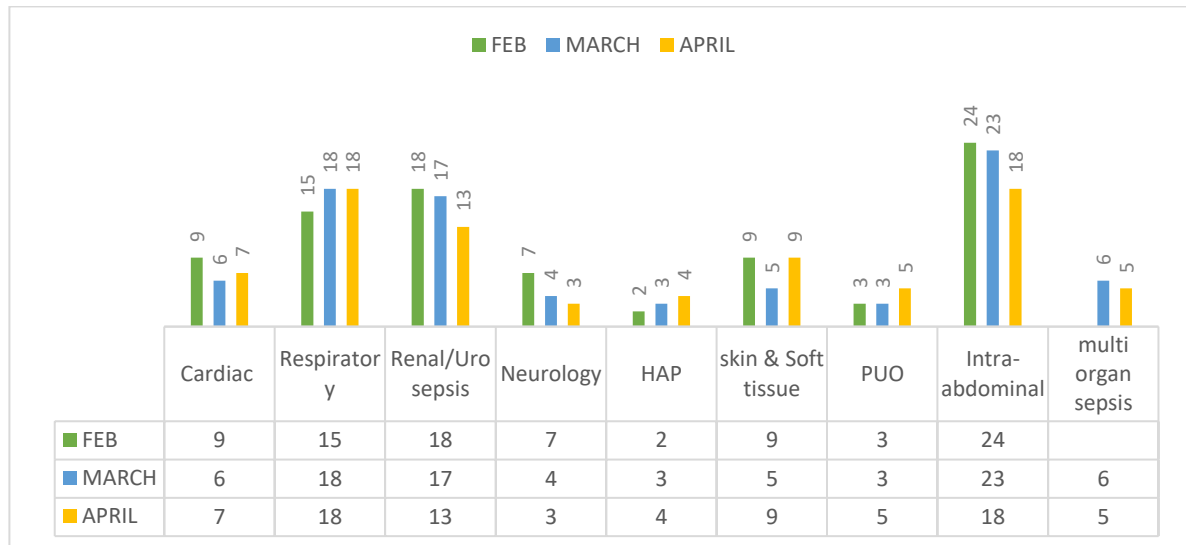


Fig:6.6 Disease pattern during the month of February, March and April

COST REDUCTION ANALYSIS IN DE-ESCALATED PATIENTS.

The total cost for each patient is calculated by multiplying the cost for one vial with the number of doses of antibiotic the patient has received. For every disease condition the organisation has defined the number of days for which the drug must be administered. This is considered as the standard treatment regimen. Anticipated cost is calculated by multiplying cost of one vial with the standard treatment regimen. Cost saved is calculated by the subtracting the total cost from the anticipated cost.

The percentage of cost saved is calculated for each drug in Meropenem , Poly B , Tigecycline and Colistin. A month wise analysis is done which shows the percentage of cost saved in April (67.5%) was higher than in February (44%) and March (57.57 %) . The percentage of total cost saved is also calculated across the drugs Meropenem , Poly B , Tigecycline and Colistin during the period February to April 2019. Poly B had the higher

percentage of cost saved (73%) while tigecycline had the minimum percentage of cost saved (54%).

PERCENTAGE OF COST SAVED			
	FEB	MARCH	APRIL
Meropenem	↓ 47	→ 51	→ 65
Tigecyclin	↓ 45	→ 50	↑ 73
Colistin	↑ 71	→ 56	→ 54
Poly B	→ 66	↑ 74	↑ 78

Fig 6.6: Percentage on Cost Saved for Meropenem, Tigecycline ,Colistin and Poly B in the month of February March and April.



when % more than 70 and above.



when % less than 49



when % between 50 - 69

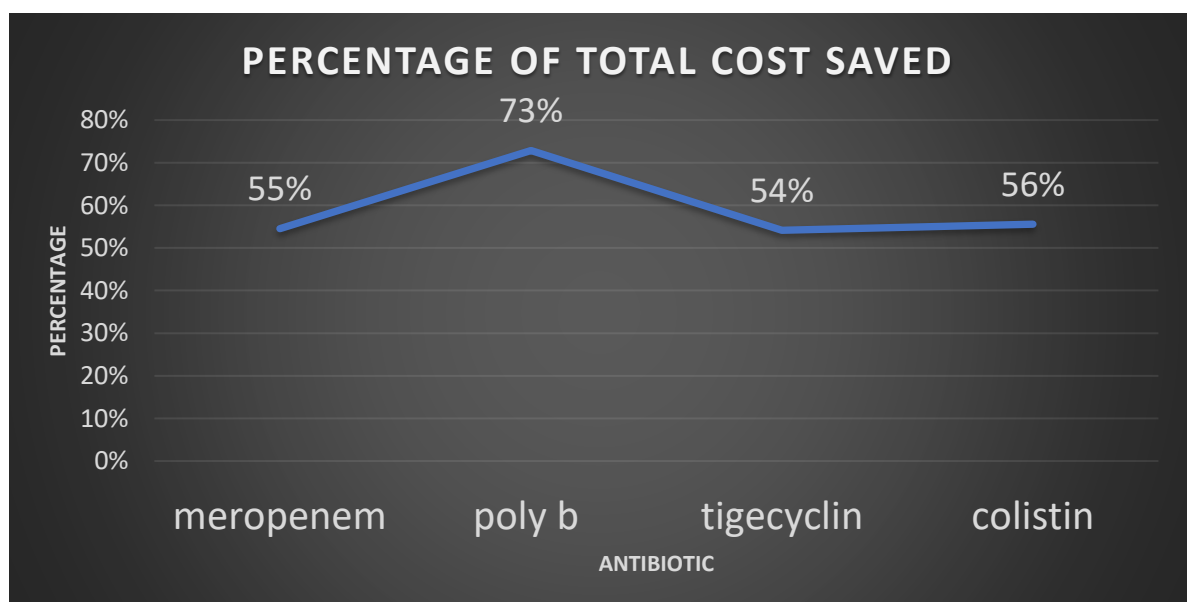


Fig 6.7: Percentage of total Cost Saved in Meropenem, Poly B, Tigecycline and Colistin .

The average cost per patient was calculated .It was found to be INR 33,000/-

RESULT :

Thus, using the indicators of Input ,Process and outcome measures, the appropriateness of Antibiotic Stewardship Program was measured.

INPUT MEASURE:

The Antibiotic stewardship program was implemented with a multi-disciplinary team involving the ICN nurses, Infectious Diseases consultants ,Clinical Microbiologist and Clinical Pharmacists . There were specific guidelines for initiating the empiric therapy of high-end antibiotics. There was a specific process defined identifying the roles of the above mentioned stakeholders in each step.

PROCESS MEASURE :

The percentage of appropriate de-escalation was calculated and was found to be 92.9%

OUTCOME MEASURE :

The Cost reduction Analysis was done in patients who were de-escalated to narrow spectrum antibiotics under empiric therapy. It was calculated for Meropenem ,Poly B, Tigecycline and Colistin.

Cost saved in

- Meropenem – 55%
- Poly B -73%
- Tigecycline -54%
- Colistin – 56%

The average cost saved per patient due to de-escalation of high-end Antibiotics is INR 33,000/-

CONCLUSION:

- The implemented Antibiotic Stewardship Program is found to be effective after reviewing the policy and guidelines and the appropriateness was measured using systems framework..
- A strong infection prevention and control program (IPC) and successful antimicrobial stewardship efforts can have reducing Multi-Drug Resistant Organisms (MDROs).
- These programs assesses the burden of MDRO's and ensures the incidence of Hospital Acquired Infection (HAI) rates are low.
- Hence the best partner for Anti-microbial Stewardship for an organisation is its

REFERENCES:

[1] <https://www.cdc.gov/infectioncontrol/guidelines/mdro/introduction.html>

[2]19. Viswanathan VK, Mallozzi MJ, Vedantam G: *Clostridium difficile* infection: An overview of the disease and its pathogenesis, epidemiology and interventions. *Gut Microbes*. 1:234–242, Jul. 2010.

[3] Ibrahim, E. H., Sherman, G., Ward, S., Fraser, V. J., & Kollef, M. H. (2000). The Influence of Inadequate Antimicrobial Treatment of Bloodstream Infections on Patient Outcomes in the ICU Setting. *Chest*, 118(1), 146-155. doi:10.1378/chest.118.1.14.

[4]Mave, V., Chandanwale, A., Kagal, A., Khadse, S., Kadam, D., Bharadwaj, R., ... Gupta, A. (2017). High Burden of Antimicrobial Resistance and Mortality Among Adults and Children With Community-Onset Bacterial Infections in India. *The Journal of infectious diseases*, 215(8), 1312–1320. doi:10.1093/infdis/jix114

[5]Jan-Willem H. Dik, Ron Hendrix, Randy Poelman, Hubert G. Niesters, Maarten J. Postma, Bhanu Sinha & Alexander W. Friedrich (2016) Measuring the impact of antimicrobial stewardship programs, *Expert Review of Anti-infective Therapy*, 14:6, 569-575, DOI: [10.1080/14787210.2016.1178064](https://doi.org/10.1080/14787210.2016.1178064)

[6] <https://www.apollohospitals.com/>

[7]<https://www.cdc.gov/antibiotic-use/healthcare/implementation/core-elements.html>

[8] www.iihmr.in