

Comparative Study on Antibiotic Stewardship and its Impact on Patient's Health: Evidence-Based and Case Studies

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Abstract:-

➤ Background

Antimicrobial abuse is connected to the emergence and dissemination of drug-resistant pathogens, as well as other problems. Morbidity, death, hospital stay periods, and healthcare costs have all risen. Antimicrobial stewardship is an overarching word for a holistic quality management approach involving evidence-based information exchange programs to optimize the usage of antimicrobials, enhance patient outcomes, minimize antimicrobial resistance, and hospital-acquired infections including *Clostridium difficile*, and lower healthcare costs. Antimicrobial stewardship program (ASP) aims to prevent or slow the emergence of antimicrobial resistance, optimize the selection, dosing, and duration of antimicrobial therapy, reduce the incidence of drug-related adverse events, and reduce rates of morbidity and mortality, length of hospital stay, and costs by evaluating and improving how antimicrobial agents are selected and delivered.

This study was conducted in three different hospitals, from each hospital 100 patient profiles were evaluated to compare the effectiveness and benefits of the antibiotic stewardship program. A pre-designed intervention form is used for the assessment to evaluate patients' profile / Computerized Physician order entries / Manual prescriptions which contain at least one or more kinds of antibiotics.

In this study, some parameters were observed as there is a total 18 number of antibiotics mostly prescribed to patients, however, in small rural hospitals there were large spectrum antibiotics were prescribed more without justification, however in tertiary care hospitals, the selection of antibiotics is based on the patient's need, beyond that it was observed that mostly drug resistance cases occur in a small rural hospital and a small urban hospital as compared to a large tertiary hospital. Further, it was evaluated that eight different Drug-related problems (prescribing) were associated with improper use of antibiotics. i.e. the excessive duration of therapy, culture sensitivity (C/S) not followed, culture sensitivity (C/S) not Reported, high dose prescribed, and therapeutic drug monitoring (TDM) not reported, Through this study that is evaluated that in large tertiary care hospitals, ASP implemented effectively so due to that there were 25257 PKR was saved on each patient which was the cost of unwanted therapy, but in a small rural hospital and the small suburban hospital where there is no any concept of ASP, and there is no any restriction to prescribe unwanted antibiotics, due to that reason there was no saved cost at these type of hospitals.

➤ Conclusion

With the help of this limited study it was concluded that in tertiary care hospitals (where ASP was implemented) there was optimum use of antibiotics, cases of bacterial resistance were not much more, and here clinical outcomes of patients were observed more but as compare to this in a small rural hospital and small suburban hospital there were unethical use of antibiotics were observed, and no any restriction and limitations are observed to

prescribe and dispense antibiotics. Instead of this, that was also observed that in tertiary care hospitals, the extra cost was saved due to short stays and proper use of antibiotics, but there was no saving in other hospitals where ASP was not implemented. So finally this is to conclude that ASP has more benefits and must be implemented in every healthcare setup.

Keywords:- Antibiotics Stewardship, Clinical Pharmacy, Pharmacoeconomics, Pharmacist.

I. INTRODUCTION

➤ Antibiotic Stewardship

The development of drugs especially antibiotics was a very successful event in the world of medicine, but parallel in the early days of antibiotics ensured that even as resistance arose, there was still a new drug available to cure the newly resistant bacteria. Between 1935 and 2003, very few antibiotics were added. On the other hand, quick antimicrobial development and antimicrobial resistance were observed. Resistance to antibiotics and antifungals raises the biggest risk in the hospitals. In 2003, US intensive care units (ICUs) confirmed to the Centers for Disease Control and Prevention that about 60 percent of *Staphylococcus aureus* isolates were immune to methicillin.[1][2] A 2010 "Centers for Disease Control and Prevention" reports that the prevalence of invasive methicillin-resistant *S aureus* infections in healthcare settings was found to be declining.[3] The rapid development and distribution in ICUs worldwide of antimicrobial-resistant microorganisms represent a Crisis Dimensions Problem. The root causes of this problem are multifactorial, however, there are strong central aspects. The development of antibiotic resistance is strongly correlated only with selective pressure occurring from excessive use of antibiotic resistance.[4][5] So In 2016, the United Nations proclaimed antimicrobial resistance "the greatest and most pressing global risk".[6] Up to this era, many researchers confirmed that this is only due to the overuse and abuse of antibiotics which drives antimicrobial resistance. [7] From many studies, it is established that unwanted and unusual use of antibiotics will increase resistance from specific species, and multiple drug treatments, which will lead to a high cost of therapy. [8][9] By using this in all hospitals, clinics will reduce misuse of antibiotics, and increase health quality and treatment that will decrease the antimicrobial resistance towards therapy.[10][11][12]

Due to the resistance of antibiotics from certain kinds of microbes WHO recognizes and declares this a rising threat,[13] so to limit the inappropriate utilization of therapy in all healthcare facilities antibiotics, these developing programs should be followed.[14][15]. Since antibiotic use and the key factor of antibiotic resistance are in facilitating judicious antibiotic use, antibiotic stewardship (AS) plays a crucial role in the violence.[16] ASP finds the patterns of resistance and controls the multiple treatments for the patients who are

receiving antibiotics, in this way adverse drug events can also be reduced. [17]

Antibiotic stewardship will specify whether it is a program or mechanism by which antibacterial antibiotics are appropriately administered, meaning that the doctor can prescribe all antibiotics at the correct dosage (individualized dose) for patients according to age, body weight, kidney function, and hypersensitivity problems.[18] He or she must also administer the necessary regimen/frequency for the patient's admiration of antibiotic medicines and antibiotics must also be administered for the correct and perfect period in reaction to such antibacterial infections to produce favorable clinical results. Any therapeutically, prophylactically, or empirically can be recommended. [19][20]. Davey et al found that ASPs are successful in minimizing the length of therapy and increasing commitment to the policy of antibiotic use in a new study of AS trials covering every continent. Nowadays ASP considers a broad and advanced strategy to rationalize the use of antibiotics, and many researchers agreed that this broad program/plan comprehensively has two goals i.e. primary goal and secondary goal. [21][22]

Primarily, ASP focused on patients' clinical outcomes and how that may be improved and the use of antibiotics minimized in such a way that as much as a desirable goal may be achieved in response to the selection of an accurate antibiotic drug to treat the infection for improvement of patient health (this is considered as a basic objective of successful ASP).[23] Secondly, ASP is engaged to decrease the cost of therapy during the stay of patients in the hospital without compromising the quality of treatment. [24][25] Beyond that ASP is a program that provides the way and makes it bound to all clinicians they write antibiotics as per antibiotic guidelines and in this way, the patients will save from polytherapy and increase cost as well, so this program is most important for all healthcare setups. [26]

➤ Desirable Goals of ASP

Many studies mentioned that there are multiple goals for ASP to achieve which are discussed below.

- An effective ASP is engaged to implement such an environment in which "an appropriate and optimum" use of antibiotics can be established.
- ASP should implement such a policy that all antibiotics are prescribed in individualized doses for the patient to treat certain microbial infections versus C/S directed antibiotic treatment.[27]
- ASP should establish treatment guidelines for clinicians and also provide feedback process in the sense of continuous education.[28]
- ASP should make a policy to survey the knowledge of every prescriber about antibiotics.[29]

- ASP organizes education programs on antibiotics, and infection treatment / clinical problems.
- ASP helps to IT department to develop software that facilitates automatic stop orders to assist in making duration more visible to in-patient pharmacists as well as clinicians. [30]

➤ *Out Comes to Measure ASP*

What is the outcome that can be measured, from some Physician's (I-D) studies; it has been extracted that the following degree circumstances should be checked by ASP.[31][32][33]

- Annually cost of hospital pharmacy is related to the procurement of antibiotics.
- Cost per patient on therapy of antibiotics.
- Evaluate compatibilities and incompatibilities among different antibiotics inpatient medication charts.
- Conversion of the route of administration from I/V to PO.
- Intervene about ADRs, and dosages to individualize doses for patients.
- Report and decide to stop extra drugs in a patient's medication chart.

II. MATERIAL & METHOD

A descriptive evidence-based study was conducted in three types of hospitals "small rural hospital, small suburban hospital, and large tertiary university hospital" [18] situated in different districts of the province of Sindh Pakistan whereas in small rural hospitals, there was no proper setup of pharmacy and medications/antibiotics are dispensed without pharmacist (without antibiotic stewardship program), and in the small suburban hospital where antibiotics were dispensed by pharmacy technician/dispenser (there was antibiotic stewardship program partially implemented), but in large tertiary care university hospital there were properly antibiotic stewardship program implemented.

From each hospital 100 patient's medication charts/profiles were intervened, only those profiles were selected in which any type of antibiotic was prescribed for certain purposes i.e. prophylaxis, empiric, therapeutic use, and all data were evaluated in the sense of goals of ASP, i.e. clinical outcomes and cost of therapy that either ASP is beneficial or not. And finally, it was compared with each other. Although the recommendations for using antibiotics that were prescribed to patients were matched with international standards books, Laxicomp (handbook of Medicine), and the British National Formulary (BNF).

➤ *Sampling*

A total number of 300 patients' profiles/prescriptions in which one or more antibiotic drugs were prescribed by the physician, were observed from three types of hospitals.[34] The profiles/prescriptions are of patients either who were admitted to the wards (in-patients) or come in an OPD (outpatients department) in the concerned organization.[35]

➤ *Study Tools and Duration of Study*

A pre-designed intervention form is used for the assessment to evaluate patients' profile / Computerized Physician order entries / Manual prescriptions which contain at least one or more kinds of antibiotics. The data was collected from the study site between the periods of February 2023 to July 2024.

III. RESULTS

➤ *Evaluation of the Social Status of the Patient whose Medication Profiles were Reviewed.*

In this section, the patient's profiles were evaluated according to social status, and observed that poor patients who belong to the rural area visited a small rural hospital in more no. i.e. 93% because of low income and locality visited the nearest hospital and in small suburban areas middle-class people visited more in number, but in large tertiary care hospitals which upper class visited more i.e. 72% because of locality and residential status although there are some patients visited who's status is poor but visited tertiary care hospital due to the severity of infections may be.

Table 1 Evaluation of Patient Profiles according to Social Status

Type of hospitals	The Financial Status of Patients		
	Poor	Middle Class	Upper Class
Small rural hospital	93%	7%	0%
Small suburban hospital	40%	55%	5%
Large tertiary university hospital	3%	25%	72%

➤ *Evaluation of Antibiotics Prescribed in Different Hospitals*

During the study, there were 300 patient profiles observed in total and it was evaluated that there is a total 18 number of antibiotics mostly prescribed to patients. Table 2 contains detailed data about the antibiotics prescribed, in which it is studied that in all

types of hospitals, ceftriaxone is prescribed in the highest i.e. 18 times in small rural hospitals and 12 times in small Suburban hospitals and large tertiary care hospitals it was prescribed in 15 times. Although it is observed that in small rural hospitals, there were large-spectrum antibiotics were prescribed in large numbers but in tertiary care hospitals, the narrow-spectrum of

antibiotics prescribed more which shows that the use of antibiotics in a tertiary care hospital based on the

patient's need. The detail is mentioned in Table 2.

Table 2 The Number of Antibiotics Prescribed in Different Types of Hospitals

Name of antibiotic prescribed	Small Rural Hospital (%)	Small Suburban Hospital (%)	Large Tertiary care Hospitals (%)
Amikacin	5	3	10
Ampicillin	10	5	0
Azithromycin	3	5	5
Cefixime	10	9	8
Ceftriaxone	18	12	15
Ciprofloxacin	4	5	5
Clindamycin	3	5	5
Co-Amoxiclav	8	5	3
Colistrimithate	0	1	3
Erythromycin	5	3	8
Gentamycin	5	7	5
Imipenem	4	9	8
Levofloxacin	7	5	5
Linezolid	0	3	1
Meropenem	3	3	10
Metronidazole	3	8	2
Pipercillin+tazobactam	5	5	2
Vancomycin	7	7	5

➤ *Evaluation of cases in which Antibiotic Resistance Developed from Certain Antibiotics Prescribed*

This is observed through this study that most resistance cases occurred in a small rural hospital, and a small suburban hospital as compared to the large tertiary care hospital where antibiotics were dispensed without the supervision of a pharmacist. However, in a

tertiary care university hospital, where ASP was fully implemented there were very less drug resistance cases observed as shown in Figure 1. which shows the ratio of cases in which drug resistance developed from susceptible microorganisms against prescribed antibiotics in different health care setups.

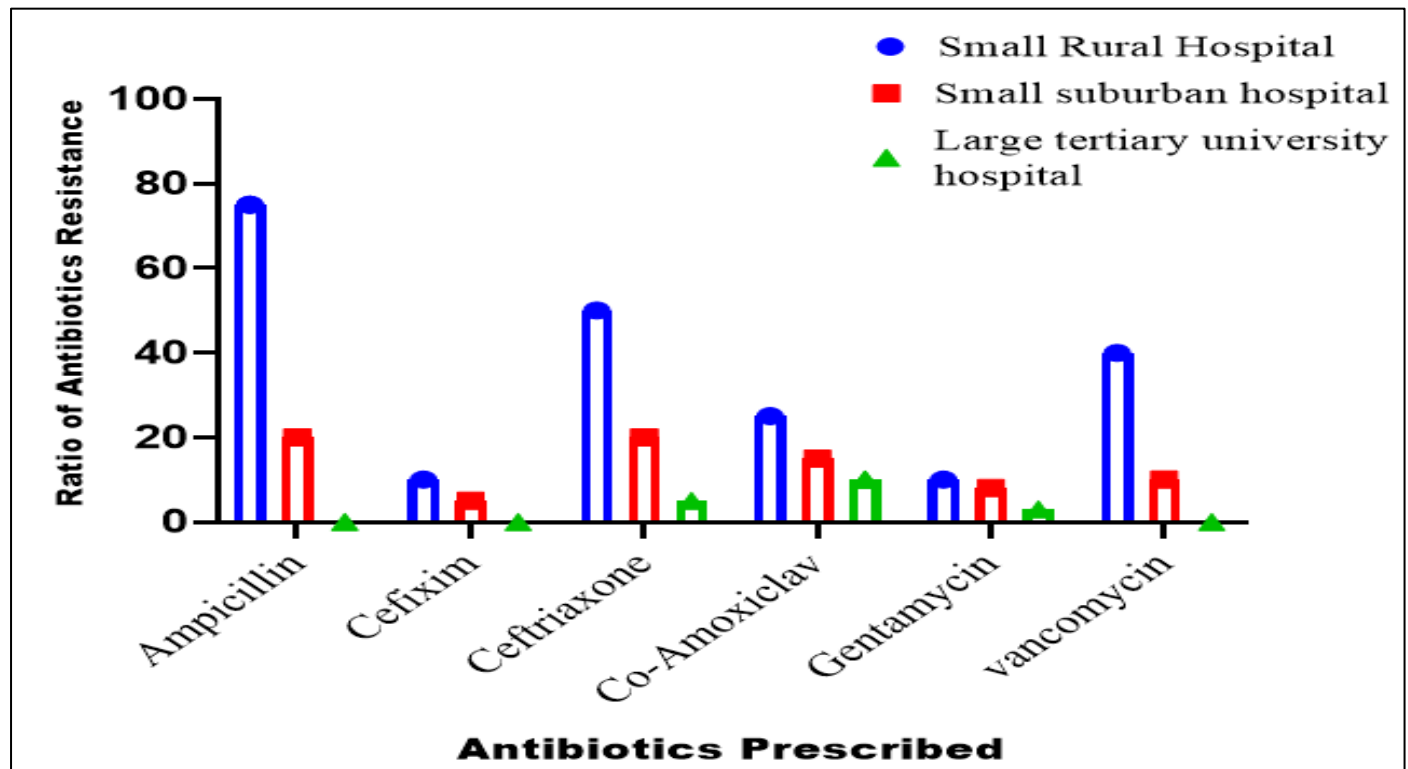


Fig 1 The Number of cases in which Drug Resistance was Developed from Certain Antibiotics.

➤ Evaluation of Patient Profiles according to Drug-Related Problems (DRPs)

It is observed that the ratio of DRPs is higher in small rural hospitals which include the excessive duration of antibiotics, C/s not reported, TDM of narrow therapeutic drugs monitoring not reported, and

antibiotics prescribed for wrong time duration etc. as shown in Figure 4. which shows the ratio of cases in which drug resistance developed from susceptible microorganisms against prescribed antibiotics in different health care setups.

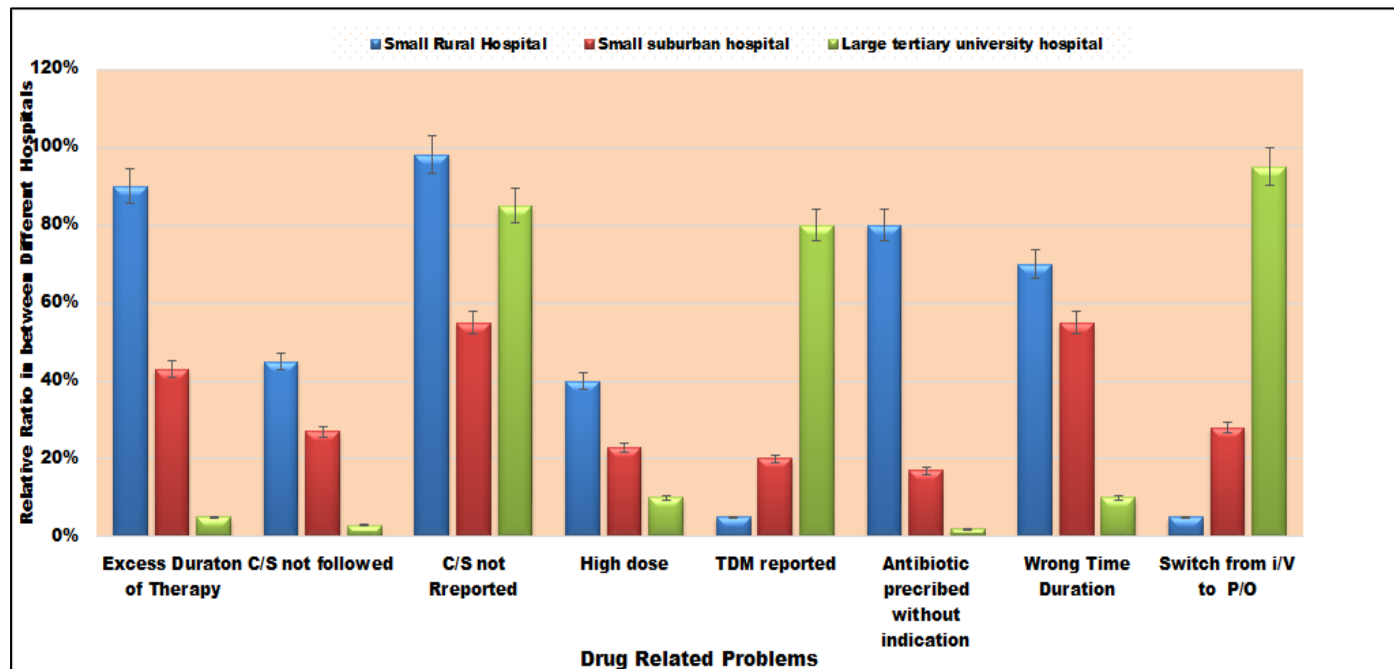


Fig 2 Evaluation of Patients Profiles according to DRPs.

➤ Evaluation of the Cost of Therapy

This is discussed earlier that the secondary goal of ASP is to decrease cost which may be because of the unwanted use of antibiotics. Through this study, it is evaluated that in large tertiary care hospitals, ASP was implemented effectively, there were 25257 PKR was saved on each patient which was the cost of unwanted therapy, but in a small rural hospital and the small

suburban hospital where there is no concept of ASP, and there is no restriction to prescribe unwanted antibiotics, due to that reason there was no saved cost at these type of hospitals. The detail is shown in Table 5. The average cost saved per patient is 25257 during the hospital stay and the maximum cost saving per patient is 30,000 PKR.

Table 3 Analysis of Cost of Therapy

Type of Hospitals	Average cost per patient per day	The cost saved per patient (Max.)	Average cost saved per patient
In a small rural hospital	20,000	0	0
In a small suburban hospital	45000	0	0
In large tertiary care hospital	80,000	30,000	25,257

- **Note:** The Cost is calculated as per retail prices of each drug which is evaluated during the study.

IV. DISCUSSIONS

This study was mainly conducted to evaluate the benefits of antibiotic stewardship programs because ASP is the only tool to overcome the improper use of antibiotics inside the hospitals and community[36], So this study was conducted from three different sites of hospitals like a small rural hospital, small suburban hospital, and large tertiary care hospital[34], where the medications/ antibiotics prescribed and dispensed without any supervision of qualified pharmacist, or

nursing staff, and where no pharmacist are involved to dispensed antibiotics and one where the pharmacist is involved in dispensing antibiotics and where ASP fully implemented respectively.[37].

The purpose of this study is to highlight the advantages of ASP to improve patients' health care, control the undesired and unusual use of antibiotics, and determine the cost which may be lower due to rational use of antibiotics.[38] Current problems about the use and misuse of antibiotics particularly large-spectrum antibiotics[39]. This study has great importance because the WHO announced that improper utilization of antibiotics is a rising threat to the world because

antibiotic resistance is produced by microorganisms and poor entry of new agents i.e. antibacterial drugs [40]. So this study was conducted from three different hospitals and consisted of a total of 300 case studies (patients profile 100 from each hospital to compare the benefits of ASP) whereas in the Wu LD et al study, 835 patients were monitored that were receiving antibiotics.[34]

In this study, different parameters were evaluated including social status, where It is evaluated that in small rural hospitals poor patients visited more, and in large tertiary care hospitals upper-class people visited more the reason may be the locality and affordability but one very important thing is that no better facilities are available in small rural and small suburban hospitals, and there is no any concept of ASP because of this, the unusual use of antibiotics are very high in the ratio which leads to increase the time of hospitality, ultimately cost of therapy increased, beyond that the risk of antibacterial resistance from susceptible micro-organisms also increased[41]. In this study, it is evaluated that two types of antibiotics either large-spectrum or narrow-spectrum antibiotics prescribed, and it was evaluated that in a small rural hospital and small suburban hospital, spectrum antibiotics were prescribed more as compared to large tertiary care hospital, were also observed that the large-spectrum antibiotics are prescribed for more time duration. But where ASP was implemented i.e. In tertiary care hospitals there was evidence-based and optimum use of large spectrum antibiotics for a limited period (maximum for 72 hrs. was observed. Instead of this similarly, Giulio DiDiodato et al study Narrow spectrum was prescribed in 559 patients from 644 patients in the medical ward and 42 patients from a total of 51 patients from the medicine ward, and Broad spectrum was prescribed in 129 patients from 143 patients in the medicine ward and 39 patients from total 43 patients in the surgery ward taking an antibiotic. In our study, different ratios of patients were Switch from I/V to P/O whereas Giulio DiDiodato et al studied 584 patients from 697 patients in the medicine ward and 57 patients from 75 patients in the surgery ward Switched from I/V to P/O. [42][43][44]

In our study intervention was required in patient profiles, like, “Excess Duration of Therapy, C/S not followed, C/S not reported, High dose, TDM reported, Antibiotic prescribed without indication, Wrong Time Duration, Switch from I/V to P/O whereas a similar study Metjian TA et al 45% prescription requires intervention through this ASP. These interventions were required in micro-organisms and their pathogens in 20% of patients, in 43 % of patients Consultation was required, in 33% of patients Optimization of antimicrobial therapy, in 4% of patient antibiotics was stopped, in 3.5 % of patients, alternative therapy was intervened by ASP. [45][46]

During the study period where ASP was implemented i.e. in tertiary care hospitals, its effects were observed in terms of cost. The average cost saved per patient was 25257 Rs, Cost saved per patient (Maximum) was 30000 Rs. [47]

Through ASP implementation, several goals were achieved in the hospital to reduce the health care problem, [48] these include decreasing the inappropriate unnecessary use of antibiotics, especially the use of broad-spectrum antibiotics. The intervention was made by implementing Asp to enhance the proper detection of infection and proper therapy for the treatment of infection.[49][50].

➤ Declaration of Competing Interest.

The authors have no conflict of interest to declare.

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