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Original Research Article

Antimicrobial Stewardship: An evidence Based Approach

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Abstract

Background: Antimicrobial stewardship (AMS) programs have shown to reduce the emergence of antimicrobial resistance (AMR) and health-care-associated infections (HAIs), and save health-care costs associated with an inappropriate antimicrobial use. ***Methods:*** This is a prospective, descriptive and observational study conducted at Department of Microbiology, Surabhi Institute of Medical Sciences over a period of 1 year included 410 patients. Patients of either sex of any age who have been admitted inward and on antibiotic therapy were included. Outdoor patients were excluded in our study. Conducted from various clinical Departments such as Medicine wards, Surgical wards, Paediatric wards and Orthopaedics wards. All data was be documented and reviewed periodically. Any deviations from the agreed criteria were communicated, discussed, and documented. ***Results:*** On the basis of gender, frequency of Male patients were recorded little bit higher (62.6%) than female (37.4%). So, the hospital attendance rate of this study was male predominant**.** Majority of subjects belonged to 21-40 years (32.1%) followed by 1-20 years (29.5%) of age range. When it is categorized according to ward, in Medicine ward was recorded 34.8%, and for Orthopaedics it was 20.0%, while 30.9% for surgery and 14.1% paediatrics wards. For this study, subjects were categorised in eighteen groups on the basis of their diagnosis. Out of which, majority of the population (20.50%) were found with diagnosis of carcinoma followed by orthopaedic diseases (19.90%), while least number of patients (0.9%) were diagnosed with ophthalmological as well as thyroid diseases. Beta lactam and Cephalosporin were found the most frequent used first antibiotic even after surgery. Even for the each wards, Beta lactam and Cephalosporin were recorded highly significant and most desirable choices among all the antibiotics. ***Conclusions:*** Implementation of a multidisciplinary antibiotic stewardship program in this academic, large, Indian hospital demonstrated feasibility and economic benefits.

Keywords: Antimicrobial resistance; antimicrobial stewardship; appropriateness; defined daily dose.

INTRODUCTION

For decades microbes, in particular bacteria, have become increasingly resistant to various antimicrobials. The World Health Assembly's endorsement of the Global Action Plan on Antimicrobial Resistance (AMR) [1] in May 2015, and the Political Declaration of the High-Level Meeting of the General Assembly on AMR in September 2017, both recognize AMR as a global threat to public health. [2] These policy initiatives acknowledge overuse and misuse of antimicrobials as a main driver for development of resistance, as well as a need to optimize the use of antimicrobials.

Antimicrobial stewardship (AMS) is a coherent set of actions which promote the responsible use of antimicrobials. This definition can be applied to actions at the individual level as well as the national and global level, and across human health, animal health and the environment [3]. Antimicrobial stewardship programs optimize the use of antimicrobials, improve patient outcomes, reduce AMR and health-care-associated infections (HAIs), and save health-care costs amongst others [4].

Many countries around the world have developed and are implementing their national action plans (NAPs) on AMR, in which AMS is a key priority. [5] Although there is a scientific evidence base for AMS, and national, regional and global guidance documents exist, there is a growing need for more specific guidance on how to establish, implement and evaluate effective AMS programs at the national and health-care-facility level [6].

AMS programs result in significant decreases in antimicrobial consumption and cost and improve infections due to specific antimicrobial-resistant pathogens and the overall hospital length of stay as well [7]. Future studies should focus on the sustainability of these outcomes and evaluate potential beneficial long-term effects of AMS programs in mortality and infection rates [8].

MATERIAL AND METHODS

This is a prospective, descriptive and observational study conducted at Department of Microbiology, Surabhi Institute of Medical Sciences over a period of 1 year included 410 patients. Patients of either sex of any age who have been admitted inward and on antibiotic therapy were included. Outdoor patients were excluded in our study.

Site of study- Conducted from various clinical Departments such as Medicine wards, Surgical wards, Paediatric wards and Orthopaedics wards. All data was be documented and reviewed periodically. Any deviations from the agreed criteria were communicated, discussed, and documented.

Antibiotic stewardship started from an in-patient setting. In the first phase, the patient pool from in-patient was addressed. For the prospective audit, two components have been recognized to have an evidence level 1. These are multidisciplinary rounds of infectious diseases patients and the use of antimicrobials. A schedule was drawn up for the following groups of patients- 1) Medical wards, 2) Surgical wards, 3) Pediatrics ward, and 4) Orthopedics ward.

Statistical Analysis

Descriptive statistics were used to summarize the key outcome data before and after the implementation of ASP. SPSS version 25 was used for all statistical analysis.

RESULTS

On the basis of gender, frequency of Male patients were recorded little bit higher (62.6%) than female (37.4%). So, the hospital attendance rate of this study was male predominant (**Table 1).**

Table 1: Gender wise frequency distribution of the population under study

Gender	No. of individuals	Frequency %
Male	257	62.6
Female	153	37.4

Table 2: Frequency of Age distribution among the study subjects

Age	No. of individuals	Frequency %
1-20 years	121	29.5
21-40 Years	132	32.1
40-60 Years	93	22.6
> 60 Years	64	15.6
Total	410	100.0

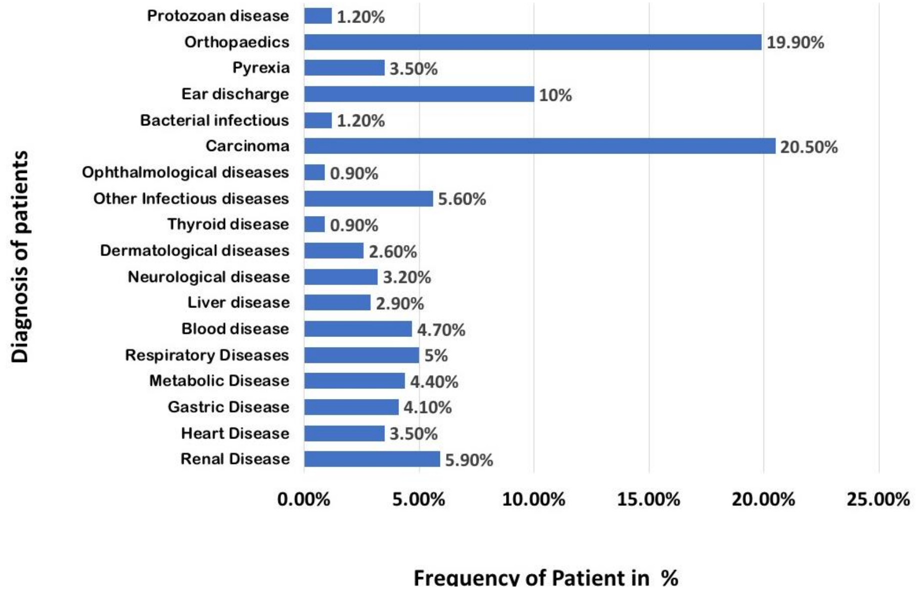
In table 2, majority of subjects belonged to 21-40 years (32.1%) followed by 1-20 years (29.5%) of age range.

Table 3: Number of patients according to each ward

Ward	**Number of patients**	**Percentage**
Medicine	143	34.8
Orthopaedics	82	20.0
Surgery	127	30.9
Paediatrics	58	14.1
Total	410	100

When it is categorized according to ward, in Medicine ward was recorded 34.8%, and for Orthopaedics it was 20.0%, while 30.9% for surgery and 14.1% paediatrics wards in Table 3.

Figure 1: Frequency distribution of the population under study in respect of diagnosis



[A] Antibiotic administration pattern

For this study, subjects were categorised in eighteen groups on the basis of their diagnosis. Out of which, majority of the population (20.50%) were found with diagnosis of carcinoma followed by orthopaedic diseases (19.90%), while least number of patients (0.9%) were diagnosed with ophthalmological as well as thyroid diseases. (**Figure: 1**).

Table 4: First Antibiotics administered among study subjects after surgery

Antibiotic class	Antibiotic	Subject administered	
		N	Frequency %
Fluoroquinolones	Norfloxacin, Ofloxacin/Ornidazole, Levofloxacin, Ciprofloxacin	13	3.1
Beta lactam	Amoxicillin Clavulanic Acid, Piperacillin / Tazobactam, Meropenem, Imipenem	162	39.5
Cephalosporin	(Cefazolin(1st Generation), Ceftriaxone (3rd Generation), Cefalexin(1st Gen) Cefixime (3rd Generation),Cefuroxime(2nd Generation), Ceftazidime (3rd Gene)	154	37.5
Broad spectrum antibiotics	Doxycycline, Tigecycline, Chloramphenicol	11	2.6
Aminoglycosides	Gentamicin, Amikacin	9	2.1
Macrolides	Azithromycin, Clindamycin, Linezolides	27	6.5
Antitubercular treatment	Pyrazinamide, Ethambutol, Isoniazid, Rifampicin, Rifamyxin	8	1.9
Antimalarial drugs	Artesunate /Sulfadoxim), Primaquine	11	2.6
Penicillin	Penicillamine, Penicillamine V, D Penicillin	9	2.1
Chloramphenicol	-	3	0.7
Other	Imatinib	3	0.7
Total		**410**	**100**

Beta lactam and Cephalosporin were found the most frequent used first antibiotic even after surgery. Even for the each wards, Beta lactam and Cephalosporin were recorded highly significant and most desirable choices among all the antibiotics in Table 4.

Table 5: Distribution of study subjects administered first antibiotics according to each ward they are enrolled

Antibiotic	Medicine (N= 143)	Orthopaedics (N=82)	Surgery (N=127)	Paediatrics (N=58)
Fluoroquinolones	9 (2.1)	0 (0)	4 (0.9)	0 (0)
Beta lactam	46 (11.2)	13 (3.1)	74 (18.0)	29 (7.0)
Cephalosporin	34 (8.2)	59 (14.3)	38 (9.2)	23 (5.6)
Broad spectrum antibiotics	11 (2.6)	0 (0)	0 (0)	0 (0)
Aminoglycosides	5 (1.2)	2 (0.4)	1 (0.2)	1 (0.2)
Macrolides	8 (1.9)	6 (1.4)	9 (2.1)	4 (0.9)
Antitubercular treatment	8 (1.9)	0 (0)	0 (0)	0 (0)
Antimalarial drugs	11 (2.6)	0 (0)	0 (0)	0 (0)
Penicillin	5 (1.2)	2 (0.4)	1 (0.2)	1 (0.2)
Chloramphenicol	3 (0.7)	0 (0)	0 (0)	0 (0)
Other	3 (0.7)	0 (0)	0 (0)	0 (0)

Table 6: Distribution of study subjects administered second antibiotics according to each ward they are enrolled

Antibiotics.	Medicine (N= 143)	Orthopaedics (N=82)	Surgery (N=127)	Paediatrics (N=58)
No drug given	81 (19.7)	55 (13.4)	105 (25.6)	44 (10.7)
Fluoroquinolones	4 (0.9)	3 (0.7)	3 (0.7)	0 (0)
Beta lactam	17 (4.1)	5 (1.2)	7 (1.7)	6 (1.4)
Cephalosporin	11 (2.6)	13 (3.1)	7 (1.7)	4 (0.9)
Broad spectrum antibiotics	9 (2.1)	1 (0.2)	0 (0.0)	0 (0.0)
Aminoglycosides	4 (0.9)	1 (0.2)	1 (0.2)	1 (0.2)
Macrolides	7 (1.7)	4 (0.9)	4 (0.0)	3 (0.7)
Antitubercular treatment	7 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
Penicillin	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)
Chloramphenicol	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)
Total	**143 (34.8)**	**82 (20.0)**	**127 (30.9)**	**58 (14.1)**

When record of study subjects were analysed for antibiotic administration according to the entire four wards they enrolled in. Most prescribed second antibiotics after the surgery was found Macrolides antibiotic, which was significantly higher than other antibiotics.

DISCUSSION

A multidisciplinary ASP was successfully deployed in this academic tertiary hospital in North India. This study helped identify ASP targets for the future and what outcomes to study in the future to improve patient care. Regulative measures such as written justification forms for restricted antimicrobials without further interaction, which were in place before the ASP was created, were largely ineffective. The reasons for ineffectiveness were multifactorial, including significant delays in reviewing the antibiotic justification forms, absence of interaction with the prescribing doctor within an actionable time frame after feedback, and lack of monitoring of compliance with feedback and duration of therapy. This signals that messaging in stewardship is important and is consistent with stewardship literature [9].

Compliance with ASP recommendations was also surprisingly high, compared with published rates of compliance [10], indicating that future directed ASP targets could have an even higher impact. Other literature has also shown that surgeons often are slow to adapt to standard ASP strategies [11], so this is a potential future targeted ASP intervention. Another future target identified from this work is de-escalation of therapy. More than half of the time, prescribers did not narrow antimicrobials when it was possible to do so, despite culture data being available. De-escalation and duration are common stewardship targets and, antimicrobial consumption, and patient outcomes [12]. This continues to be an ongoing target for our ASP, especially given the increasingly resistant Gram-negative infections seen in the patient population at this institution and broadly in Indian hospitals.

Because AMR has been such a significant threat in India, stakeholders are interested in understanding gaps in training that could be worsening the problem. The Indian Council of Medical Research (ICMR) identified lack of trained clinical pharmacists as a gap in improving antimicrobial stewardship practices in India in 2015 [13]. Clinical pharmacists have an established role within hospitals as promoters of evidence-based medicine and cost-effective prescribing [14]. Having a clinical pharmacy training program in this institution facilitated the inclusion and mentoring of trained graduates in the ASP, which was novel. With clinical pharmacists driving ASP worldwide, our experience also confirms the success of a multidisciplinary model involving clinical pharmacists who utilize their expertise to optimize antimicrobial treatment to promote rational prescriptions and reduce inappropriate prescriptions [15]. Mandating multidisciplinary ASPs in acute care hospitals would be a wise next step for policy in India and would mirror antimicrobial stewardship policy work in the United States [16].

This study has several limitations. This sample is a small sample from one organization, which limits generalizability of our findings; however, we believe that the methods used can be generalized to other sites. As such, another focus group is planned at another medical center. It is possible that study participants did not include all perspectives on the choices for selecting antibiotics. Similarly, trainee physicians with less experience may be less knowledgeable about the reasons for selecting particular antibiotics than our study population, and so might need additional links for further information or more explanation of the reasons for selecting antibiotics Therefore, we will target their participation in future usability studies with the clinical decision support interface. This focus group was limited to sixty minutes, and some factors might have changed with more discussion. However, the findings from the survey and focus group differed, possibly indicating that discussion and reflection may impact the selection of medications for the clinical decision support tool.

CONCLUSIONS

In conclusion, this work demonstrated successful implementation of a multidisciplinary ASP team in a large hospital in North India. The ASP effectively implemented several stewardship interventions including post prescriptive auditing and feedback and identified multidisciplinary stewardship champions. Our preliminary results with an ASP in India are encouraging, but a national effort to initiate, implement, and maintain ASPs in acute care hospitals needs to be studied in India. Clinical pharmacists were critical to the success of this ASP and were uniquely empowered in our center, which is an uncommon model in India. Further work empowering academic pharmacists to take part in antimicrobial stewardship in acute care inpatient hospitals in India should be undertaken.

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