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Original Article

Antimicrobial use and antimicrobial resistance in nosocomial pathogens at a tertiary care hospital in Pune

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ARTICLE INFO

Article history:

Received 15 October 2014

Accepted 28 December 2014

Available online 26 February 2015

ABSTRACT

Background: Resistance to antimicrobial agents is emerging in wide variety of nosocomial and community acquired pathogens. Widespread and often inappropriate use of broad spectrum antimicrobial agents is recognized as a significant contributing factor to the development and spread of bacterial resistance. This study was conducted to gain insight

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<http://dx.doi.org/10.1016/j.mjafi.2014.12.024>

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Keywords:

Hospital acquired infection
Antibiotic sensitivity
Antifungal sensitivity
Microorganisms
Antimicrobial use

into the prevalent antimicrobial prescribing practices, and antimicrobial resistance pattern in nosocomial pathogens at a tertiary care hospital in Pune, India.

Methods: Series of one day cross sectional point prevalence surveys were carried out on four days between March and August 2014. All eligible in patients were included in the study. A structured data entry form was used to collect the data for each patient. Relevant samples were collected for microbiological examination from all the clinically identified hospital acquired infection cases.

Results: 41.73% of the eligible patients (95% CI: 39.52–43.97) had been prescribed at least one antimicrobial during their stay in the hospital. Beta-lactams (38%) were the most prescribed antimicrobials, followed by Protein synthesis inhibitors (24%). Majority of the organisms isolated from Hospital acquired infection (HAI cases) were found to be resistant to the commonly used antimicrobials viz: Cefotaxime, Ceftriaxone, Amikacin, Gentamicin and Monobactams.

Conclusion: There is need to have regular antimicrobial susceptibility surveillance and dissemination of this information to the clinicians. In addition, emphasis on the rational use of antimicrobials, antimicrobial rotation and strict adherence to the standard treatment guidelines is very essential.

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Introduction

Antimicrobial resistance (AMR) is a natural biological phenomenon and its emergence is a complex problem driven by many interconnected factors, in particular the use and misuse of antimicrobials. Resistance costs money, livelihoods and lives and threatens to undermine the effectiveness of health delivery programs.¹ Resistance to antimicrobial agents is emerging in a wide variety of nosocomial and community acquired pathogens.² Widespread and often inappropriate use of broad spectrum antimicrobial agents is recognized as a significant contributing factor to the development and spread of bacterial resistance.³ The Indian scenario too, is dismal with regard to antimicrobial prescribing and publications have documented the irrational prescribing patterns in various settings.^{4,5}

Selective antimicrobial pressure is more in a hospital setting. Antimicrobials are prescribed in a community but not as intensively as in a hospital setting.⁶ As antimicrobial use generally precedes the emergence of antimicrobial resistance, preventing the emergence and spread of antimicrobial resistant pathogens clearly requires optimizing antimicrobial use.⁷

Hospitals need to monitor antimicrobial use in an attempt to reduce the emergence and spread of antimicrobial resistant pathogens.⁸ World Health Organization (WHO) highlights the

establishment of effective, epidemiologically sound surveillance of antibiotic use and AMR among common pathogens in the community, hospitals and other health-care facilities as one of the key public health priorities.⁹ Limited literature is available regarding antimicrobial resistance in nosocomial pathogens from our country. The present study was conducted to gain insight into the prevalent antimicrobial prescribing practices; and antimicrobial resistance pattern, in hospital acquired infection organisms, at a tertiary care hospital in Pune, India.

Material and methods

A cross sectional study, comprised of four point prevalence surveys (PPS), was conducted during March–August, 2014 at a

Table 1 – Study population of patients.

Round	R1	R2	R3	R4	Total
Date	28 Mar 14	06 May 14	27 May 14	08 Jul 14	
Total	501	553	558	507	2119
Eligible	461	491	490	444	1886
HAI	27	24	13	7	71

Fig. 1 – Demographics of the survey population.

Table 2 – Distribution of antimicrobial groups as per indication of use.

Antimicrobial groups	Treatment of infection n (%)	Medical prophylaxis n (%)	Surgical prophylaxis n (%)	Total
Beta-Lactams (Penicillins & Cephalosporins)	322 (43.5)	60 (8.1)	359 (48.4)	741
Protein Synthesis Inhibitors (Tetracyclines, Aminoglycosides Macrolides & Oxazolidones)	210 (44.4)	26 (5.5)	237 (50.1)	473
Anti TB & Leprosy	195 (100)	0 (0)	0 (0)	195
Antiprotozoal & Anti Helminths	74 (44.6)	40 (24.1)	52 (31.3)	166
Fluoroquinolones	90 (68.7)	15 (11.5)	26 (19.8)	131
Antivirals	107 (97.3)	2 (1.8)	1 (0.9)	110
PABA Synthesis Inhibitors (sulphonamides)	36 (62.1)	20 (34.5)	2 (3.4)	58
Antifungals	38 (79.2)	7 (14.6)	3 (6.2)	48
Polypeptide antibiotics	13 (92.9)	0 (0)	1 (7.1)	14
Antimalarial	4 (100)	0 (0)	0 (0)	4

tertiary care hospital in Pune. PPS surveys were done to estimate (hospital acquired infection) HAI prevalence and antimicrobial usage among in-patients. The study subjects included all in-patients of the hospital at 08:00 h on the days of surveys. Patients admitted less than 48 h prior to the time of respective survey were excluded from the point prevalence survey.

Ethical approval was obtained from the institutional ethics committee. A written informed consent was obtained from each patient.

A structured data entry form was used to collect the data for each patient. It comprised of patient demographic data, consultant speciality, ward-wise location, diagnosis, antimicrobials used and presence of HAI risk factors. Generic name, days of use, route of administration and indication of use was recorded for each antimicrobial used in individual patients during their current stay in the hospital. HAI patients were identified on the basis of HAI definition as per CDC guidelines. All operational definitions as well as codes for various parameters were included in the questionnaire itself. A pilot study was conducted in two wards during December 2013, to validate the questionnaire, and the related customised database software.

Thirteen teams of surveyors were designated. Each team comprised of residents from Departments of Medicine, Surgery, Microbiology, Community medicine, Hospital administration; and Medical Officer in charge and Nursing Officer in charge of the respective wards. The teams had access to all relevant patients' medical documents, as well as the treating physicians/surgeons. Adequate pre-survey training was imparted to all the survey teams.

Four rounds of PPS for HAI and antimicrobial usage were done on 28 Mar, 06 May, 27 May and 08 Jul 2014 respectively.

Relevant samples as per the HAI type were collected for microbiological examination from all the identified HAI cases. Processing of samples was done as per standard microbiology protocols.¹⁰

We performed the Antibacterial Susceptibility Testing (ABST) by Vitek 2 compact (Biomerieux) automated system for identification and antimicrobial susceptibility testing of microorganisms.

The antifungal susceptibility testing was also performed using the same instrument using the fungal susceptibility cards.

Fig. 2 – Commonly prescribed antimicrobial groups.**Table 3 – Most commonly prescribed antimicrobials.**

Sr no	ATC codes	Antimicrobial	Total (%)
1	J01DD01	Cefotaxime	198 (10.20)
2	J01DD04	Ceftriaxone	172 (8.86)
3	J01GB06	Amikacin	154 (7.93)
4	J01XD01	Metronidazole	147 (7.57)
5	J01GB03	Gentamicin	130 (6.70)
6	J01CR02	Amoxicillin + Clavulanic A	99 (5.10)
7	J01DD12	Cefoperazone	79 (4.07)
8	J01MA12	Levofloxacin	69 (3.55)
9	J01XA01	Vancomycin	63 (3.24)
10	J01CR05	Piperacillin + Tazobactam	49 (2.52)
11	J01MA02	Ciprofloxacin	47 (2.42)
12	J01XA02	Teicoplanin	42 (2.16)
13	J01DH51	Imipenem Cilastin	37 (1.90)
14	J01DH02	Meropenem	35 (1.80)
15	J01EE01	Cotrimoxazole	31 (1.59)

Fig. 3 – Most commonly prescribed antimicrobials.

Statistical methodology: The questionnaire of the PPS was thoroughly scrutinized and edited to ensure consistency of data in all the rounds. Statistical analyses were carried out using statistical software SPSS version 22.0.

Results

Study population

A total of 1886 patients were eligible for HAI surveys as per the inclusion criteria, during four rounds (R1–R4), as shown in Table 1.

Demographics of the study population

Among the eligible patients, 77.3% were males and 22.7% were females. The median age of all patients was 35 years (Inter-quartile range (IQR) 26–51 years). The population pyramid displayed (Fig. 1) demonstrates the distribution of patients as per age and sex.

HAI prevalence

71 patients among the eligible were detected to have an HAI clinically. Thus the overall prevalence of HAIs was 3.76% (95% CI = 2.97, 4.69). Out of them 32 had positive microbiology report.

Antimicrobial use

787 patients out of 1886 eligible patients, 41.73% (95% CI 39.52, 43.97) had been prescribed at least one antimicrobial during their stay in the hospital. A total of 1940 antimicrobials had been prescribed. These antimicrobials have been listed group-wise in Table 2.

Use of antimicrobial on a patient was classified on the basis of indication. More than half of the antimicrobials prescribed were for treatment of existing infections; followed by surgical prophylaxis as shown in Table 2.

Beta-lactams (38%) were the most prescribed antimicrobials, followed by Protein synthesis inhibitors (24%) as shown in Fig. 2.

Most commonly prescribed individual antimicrobials are classified as per WHO Anatomical, Therapeutic and Chemical (ATC) classification system as shown in Table 3 and shown in (Fig. 3). Preferred antimicrobials by different consultant specialties are shown in (Fig. 4).

30.36% of the patients with antimicrobial prescription were prescribed single antimicrobial, 31.76% with two, 21.09% with three and remaining 16.77% patients with four or more antimicrobials respectively.

Antibiotic Sensitivity Test (ABST) and antifungal sensitivity test of isolates

Majority of the organisms isolated from HAI cases were found to be resistant to the commonly used antimicrobials viz: Cefotaxime, Ceftriaxone, Amikacin, Gentamicin and Monobactams, but were sensitive to higher antimicrobials like Vancomycin, Teicoplanin, Colistin and Polymyxin B. It has been observed that even though antimicrobials like Chloramphenicol and Tetracycline are not being prescribed much these days, but many of the isolated organisms were found to be sensitive to them (Tables 4 and 5).

Discussion

The present study has found Point prevalence of HAI to be 3.76% (95% CI = 2.97, 4.69), which is lower than the rates reported by other hospitals in many developing countries. Recent systematic reviews have estimated hospital-wide prevalence of HAIs in high-income countries at 7.6% and in low and middle-income countries at 10.1%.¹¹ This might be due to significant number of chronic patients being treated in hospital wards like psychiatry, dermatology and other life-style diseases.

In our study, prevalence of antimicrobial use (AMU) was found to be 41.73% (95% CI: 39.52–43.97). Similar study by the

Fig. 4 – Antimicrobial preference by consultant specialties.

European Centre for Disease Prevention and Control (ECDC) reported AMU prevalence to be 34.6% (95% CI: 33.94–35.26).¹²

The most widely used antimicrobial group was beta-lactams (38%); 29.6% of which was intended for treatment, 35.29% for medical prophylaxis and 52.7% for surgical prophylaxis.

Ceftriaxone, Piperacillin + Tazobactam, Amikacin, AmoxiClav and Cefoperazone were among the most commonly prescribed antimicrobials by Medicine & Paediatrics specialties, even though most of the isolates were found to be resistant to them. Similarly Cefotaxime, Gentamicin, Amikacin and Metronidazole were the most commonly prescribed antimicrobials for surgical prophylaxis by specialties like Surgery, Obstetrics-Gynaecology and Orthopedics, but majority of the organisms isolated were found to be resistant to them.

ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species) pathogens were responsible for 24/38 (63.16%) of HAIs in our study. Nosocomial pathogens, such as *Enterococcus faecalis* and *Acinetobacter* species, are virtually untreatable due to multiple resistances. Similar results were obtained in some US hospitals.^{13,14} As seen in some other studies, microorganisms of HAI have more resistant profile than community acquired infection.¹⁵

Majority of the isolated organisms were found sensitive to Tetracyclines and Chloramphenicol, which are not routinely prescribed these days. Use of antimicrobials like Tetracyclines is advocated in community acquired infections to prevent emergence of resistance to other commonly used antimicrobials like Beta-lactam and Fluoroquinolones.

Several limitations need to be acknowledged for this study. It was conducted in a single hospital in a selected area. The small number of samples was examined microbiologically (Only samples collected from clinically detected HAI cases) and may affect the validity of conclusions drawn. The one time prevalence study nature may have influenced the prevalence rate and not depict the true rate as also the inability to determine the causality factors. However compared to time consuming and costly resource intensive incidence studies, repeated prevalence surveys are practical and efficient method of measuring trends over time. This methodology can be applied to any type of health-care institution including long-term care facilities.

Conclusion

There is a need to emphasize on the rational use of antimicrobials and strict adherence to the standard treatment guidelines. In addition, regular antimicrobial susceptibility surveillance and antimicrobial rotation is essential. The WHO Global Strategy defines the appropriate use of antimicrobials as the cost-effective use of antimicrobials which maximizes clinical therapeutic effect while minimizing both drug-related toxicity and the development of antimicrobial resistance.

Table 4 – Antifungal sensitivity test of isolates.

Causative Organism (n)	Amphotericin B		Caspofungin		Flucytosine		Fluconazole		Voriconazole	
	S	R	S	R	S	R	S	R	S	R
Candida parapsilosis (1)	1		1		1		1		1	
Candida albicans (2)		2	2		2			2		2
Candida tropicalis (1)		1	1		1			1		1
Non Albican Candida (3)	1				1		1		1	

Note.

n = number of specimens

S= Sensitive; R= Resistance; Blank= Not tested for the specific antifungal

Table 5 – ABST of isolates.

	Amikacin	Meropenem	Chloramphenicol	Ciprofloxacin	Clindamycin	Cotrimoxazole	Nitrofurantion	Erythromycin	Gentamicin	Levofloxacin	Linezolid	Piperacillin-tazob	Oxa/Methicillin	Penicillin	Tetracycline	Teicoplanin	Tigecycline	Vancomycin	Colistin	Imipenem	Ampicillin	Amoxiclav	Cefuroxime	Ceftriaxone	Cefotaxime	Cefepime	Cefepirazon									
Causative Organism	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R								
Staph aureus (3)	1				2	2	1	2	1	1	2	1		2	1	2	1	2	1	3																
Staph epidermidis (3)	2	1		3			2	1	2		3			2	1	2	1	1	2	3																
Staph intermedius (1)		1		1		1		1		1	1	1		1		1	1		1																	
Staph hominis (1)					1		1	1	1		1			1			1	1																		
Enterofaecalis (2)				2		2				2	2	2				2	2	2		2																
E Coli (3)	1	1	2	1		3			2	1			2	1			1			2	2	1		3	1	1	2	3	1	2	1					
Klebsiella pneumonia (6)	3	3	4	1	1		4			2	4	1	4		3	3	1		5			1		3	2	5	4	1	5	5	5	5	1	5	1	4
Klebsiella oxytoca (1)	1			1		1					1			1		1				1				1			1				1					
Serratia marcescens (1)		1		1				1	1			1					1			1	1		1	1	1	1	1		1		1		1			
Acinet baumannii (4)		1			4		4	3		4	1		2			1		3		3		3		3	4	1	4	2				4		2		
Proteus mirabilis (4)	1	3		2	2	4		2		4	1	1	4				1		1		2	3	4	1	2	4		4	2				4	2		
Proteus vulgaris (1)		1		1		1				1		1								1	1			1			1				1					
Pseud aeruginosa (6)		6	1	3		6		4	3		6	1		3			4		6	1	5															
Alkaligenes fecalis (1)		1			1							1							1						1						1					
Aeromona hydrophila (1)		1	1					1	1		1						1		1	1		1	1	1	1								1			

Note. n = number of specimens S= Sensitive R= Resistance Blank= Not tested for the specific antimicrobial

Conflicts of interest

All authors have none to declare.

Acknowledgements

Declaration of AFMRC Project: This paper is based on Armed Forces Medical Research Committee Project No 4477/2013 granted by the office of the Directorate General Armed Forces Medical Services and Defence Research Development Organization, Government of India.

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REFERENCES

1. WHO global strategy. Containment of Antimicrobial Resistance. 2010.
2. Tenover FC. Development and spread of bacterial resistance to antimicrobial agents: an overview. *Clin Infect Dis*. 2001;3(suppl 3):S108–S115.
3. Tenover FC, McGowan Jr JE. Reasons for the emergence of antimicrobial resistance. *Am J Med Sci*. 1996;311:9–16.
4. Srishyla MV, Nagarani NA, Venkataraman BV. Drug utilization of antimicrobials in the in-patient setting of a tertiary hospital. *Indian J Pharmacol*. 1994;26:282–287.
5. Das AK, Roy K, Kundu KK, et al. Study of rational utilization and cost analysis of Antimicrobials in a government teaching hospital. *Indian J Pharmacol*. 2002;34:59–61.
6. Vander Stichele RH, Elseviers MM, Ferech M, Blot S, Goossens H. Hospital consumption of antibiotics in 15 European countries: results of the ESAC retrospective data collection (1997–2002). *J Antimicrob Chemother*. 2006;58:159–167.
7. Fridkin Scott K, Steward Christine D, Edwards Jonathan R, et al. Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: project ICARE phase 2. *Clin Infect Dis*. 1999;29:245–252.
8. Goldmann DA, Weinstein RA, Wenzel RP, et al. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals. *JAMA*. 1996;275:234–240.

9. WHO publication. *The Evolving Threat of Antimicrobial Resistance: Options for Action*. 2012.
10. Mackie and McCartney *Practical Medical Microbiology*. 14th ed. India: Churchill Livingstone; 2011:95–110.
11. Ogowang M, Paramatti D, Molteni T, et al. Prevalence of hospital-associated infections can be decreased effectively in developing countries. *J Hosp Infect*. 2013;84:138–142.
12. Zarb P, Coignard B, Griskeviciene J, et al. The European Centre for Disease Prevention and Control (ECDC) pilot point prevalence survey of healthcare-associated infections and antimicrobial use. *Euro Surveill*. 2012;17:1–16.
13. Handwerger S, Raucher B, Altarac D, et al. Nosocomial outbreak due to *Enterococcus faecium* highly resistant to vancomycin, penicillin, and gentamicin. *Clin Infect Dis*. 1993;16:750–755.
14. Levin ASS, Mendez CMF, Sinto SI, et al. An outbreak of multiresistant *Acinetobacter baumannii* in a university hospital in São Paulo, Brazil. *Infect Control Hosp Epidemiol*. 1996;17:366–368.
15. de Man P, Verhoeven BA, Verbrugh HA, Vos MC, van den Anker JN. An antibiotic policy to prevent emergence of resistant bacilli. *Lancet*. 2000;355:973–978.