Journal of Hospital Infection 103 (2019) 280–283

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Short report

Variations in antibiotic use across India: multi-centre study through Global Point Prevalence survey

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A R T I C L E I N F O

Article history:
Received 8 January 2019
Accepted 28 May 2019
Available online 3 June 2019

Keywords:
Medical prophylaxis
Surgical prophylaxis
Quality indicators
Antibiotic stewardship

S U M M A R Y

The aim of the study was to assess antimicrobial prescribing patterns, and variation in practice, in India. A point prevalence survey (PPS) was conducted in October to December 2017 in 16 tertiary care hospitals across India. The survey included all inpatients receiving an antimicrobial on the day of PPS and collected data were analysed using a web-based application of the University of Antwerp. In all, 1750 patients were surveyed, of whom 1005 were receiving a total of 1578 antimicrobials. Among the antimicrobials prescribed, 26.87% were for community-acquired infections; 19.20% for hospital-acquired infections; 17.24% for medical prophylaxis; 28.70% for surgical prophylaxis; and 7.99% for other or undetermined reasons. Antibiotic prescribing quality indicators, such as reason in notes and post-prescription review score, were low. This PPS showed widespread antibiotic

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https://doi.org/10.1016/j.jhin.2019.05.014

Empirical antimicrobial therapy
Targeted antimicrobial therapy

usage, underlining the need for antibiotic stewardship to promote evidence-based practice.

Introduction

Antimicrobial resistance (AMR) is increasing across the globe, posing a major threat; this is especially so for developing countries such as India, where the burden of AMR and infectious diseases is very high [1,2]. It has been well established that antimicrobial overuse and misuse are the major driving forces for development of such high rates of resistance [3]. However, antibiotic consumption is increasing worldwide, driven by rising incomes, health insurance, and burden of infectious disease. Between 2000 and 2010, antibiotic consumption in 71 countries increased by 36%, with Brazil, Russia, India, China, and South Africa (BRICS) accounting for three-quarters of this increase [1].

Antimicrobial point prevalence surveys (PPSs) are a tool to understand antimicrobial consumption and its resistance pattern in healthcare organizations. Surveillance of antimicrobial use in hospitals can provide an insight into patterns of antimicrobial use, help highlight differences in prescribing practices among hospitals, and identify opportunities for improvement [4].

Methods

Study design and setting

A meeting of all champions from 25 hospitals across India was planned on the Global Point Prevalence Survey (Global-PPS) of Antimicrobial Consumption and Resistance developed by University of Antwerp, Belgium. Out of these 25 hospitals only 16 healthcare organizations obtained approval from their ethics committee to participate in the study. All 16 healthcare organizations were private, multi-specialty, tertiary-care accredited hospitals spread across the country with bed numbers ranging from 300 to 1350.

Data were collected from medical, surgical wards, and intensive care units. Each hospital had a unique identification number in accordance with its name, geographic location and type of hospital. All study data were completely anonymized, and no unique identifiers were recorded.

Data collection

All inpatients in the ward at 08:00 were included. Total ward inclusion at the hospital level was requested but not mandatory (Supplementary Appendix A). Data collection was done with two forms, one for ward-level data (i.e. recording of denominators, such as the total number of inpatients on the ward) and one for patient-level data (recording of numerators; Supplementary Appendices A and B). For each patient receiving at least one antimicrobial, data were gathered about patient characteristics, the antimicrobials received, their diagnosis, and the therapeutic indication according to predefined lists (Supplementary Appendix A). Two major categories – treatment and prophylaxis – were used, each of which consisted of two main types of indication. The former category comprised therapeutic antimicrobial prescribing for both community-acquired (an infection with a date of onset $\leq$2 calendar days after the hospital admission date and admitted from home/community) and healthcare-associated infections (infections with an onset date $>$2 calendar days after hospital admission date). The latter category included antimicrobial prescribing for both surgical and medical prophylaxis. Medical prophylaxis refers to medication or a treatment designed and used to prevent an infection from occurring. Surgical antibiotic prophylaxis is defined as the use of antibiotics to prevent infections at the surgical site. For patients receiving surgical prophylaxis, administration had to be checked in the previous 24 h to encode the duration of prophylaxis as either one dose, one day (i.e. multiple doses given in one day), or more than one day. The categories other than treatment and prophylaxis included other indications (e.g. erythromycin as a motility agent) or completely unknown indication.

Indicators of antimicrobial-prescribing quality included documentation of the diagnosis in the patient's notes at the start of treatment, the choice of antibiotic being compliant with local guidelines, and documentation of a stop or review date for the antimicrobial in the notes. Additionally, empirical or targeted treatment (i.e. based on microbiology data from a relevant clinical specimen, such as blood or sputum, excluding screening tests) was recorded. When treatment choice was made on the basis of available microbiology reports, a record of one of the nine targeted multidrug-resistant organisms was made (Supplementary Appendix B). All antimicrobials were automatically classified online according to the standardized and internationally recognized World Health Organization anatomical therapeutic chemical classification system ATC-DDD (2014 version) [5].

Data analysis

The focus was on prescription of antibiotics for systemic use, which was reported as number of treated patients, the number of therapies, and the number of prescriptions. Therapy was defined as one treatment (i.e. receiving at least one antibiotic) per diagnosis. A prescription was defined as the use of one substance by one route of administration. Antimicrobial prescribing rates were expressed as a percentage of patients on antimicrobials, or as a percentage of all antibiotic or antimicrobial prescriptions (proportional use).

Results and discussion

This is the first study performed across multiple tertiary care hospitals in India to assess the variation in antibiotic use. In all, 1750 patients across 16 healthcare organizations were

Table I
Ten most frequent diagnoses to be treated with therapeutic antimicrobials (2017)

Diagnosis	Frequency (%)
Skin and soft tissue	7.6
Cardiovascular system infections	5.5
Pneumonia or lower respiratory tract infection	19.9
Bronchitis	5.9
Other	3
Infection of central nervous system	6.6
Obstetric/gynaecological infections	1.7
Upper respiratory tract infection	1.1
Bone/joint infections	1.1
Intra-abdominal sepsis	4.9

included, with 1005 (57.4%) receiving at least one antimicrobial. This prevalence is compared to the data collected as a part of the Global-PPS (2015) worldwide; across 53 countries the prevalence of antimicrobial usage was 34.4% [6]. However, this overall prevalence masks important regional differences: 2017 data showed that among 68 hospitals in East and South Asia the prevalence of antimicrobial use was 48.2%, compared with 29.6% in 106 European hospitals. There have been few previous studies in India. However, our data are comparable to a study in Eastern India, which reported antimicrobial use prevalences of 62% in 2014 and 69.1% in 2017 [7]. There is no debate that the rate of antimicrobial prescribing in India is high compared to many other countries, which is a concern that requires addressing urgently.

The treated population received a total of 1578 antimicrobials. Among the antimicrobials prescribed as treatment, 424 (26.87%) were prescribed for community-acquired infections and 303 (19.20%) were prescribed for healthcare-associated infections. Overall, 358 (84.4%) antimicrobials were prescribed as empirical therapy; however, the proportion of antimicrobial agents prescribed empirically for healthcare-associated infections was lower at 65.2%. Regarding prescriptions, 272 (17.24%) and 453 (28.70%) were for medical and surgical prophylaxis, respectively. Finally, 58 (3.68%) antimicrobials were prescribed for other indications and 68 (4.3%) were prescribed for unknown indications.

The proportions of antimicrobial prescriptions that were for both medical and surgical prophylaxis were higher than in many other studies. For example, the ESAC PPS data conducted in 20 European hospitals reported rates of 15% for medical prophylaxis and 6.7% for surgical prophylaxis [8]. The high rates in our study may be partly due to the hospital types and patient cohort taken for the study, but local prescribing practices are likely also to have played a role. The patient population included patients in intensive and critical care settings, or those who were immunosuppressed. Local policies and procedures promoted antimicrobial prophylaxis for recurrent urinary tract infections, and to prevent central nervous system infections (e.g. in road traffic accident patients after intracranial procedures) and to prevent sepsis in patients with neutropenia and hepatic failure.

Ceftriaxone (24%), piperacillin–tazobactam (8%), and meropenem (8%) were the antimicrobials most frequently prescribed for medical prophylaxis. The use of such broad-spectrum antimicrobials as prophylaxis was driven by the real or perceived high prevalence of antibiotic resistance in Enterobacteriaceae and non-fermenting Gram-negative bacteria.

There were 94 (19.9%) pneumonia or lower respiratory tract infections (LRTIs) among patients treated with at least one antimicrobial; the next most frequent was skin and soft tissue infection (Table I). This is consistent with the Global-PPS 2015 study (19.2%), where, except in Africa, all other subregions reported a high proportion of patients with LRTI [6]. As per our study, the most frequently used antibiotics used for pneumonia were piperacillin–tazobactam (18%) followed by meropenem (16%) and azithromycin (9%).

Penicillins together with β-lactamase inhibitors (47.6%) were the most frequently used antibacterials in our study, which is similar to a large study conducted in Southern, Northern, Western Europe, East and South Asia, and Oceania subregions (accounting for 24.8% of the total antimicrobial prescriptions across the globe) [6]. Other authors have also reported penicillins with β-lactamase inhibitors (24%) as the most frequently prescribed antibiotics [8]. This high prevalence of use may be due to a perception that these antibiotics are effective against extended-spectrum β-lactamase (ESBL)-producing Gram-negative bacteria that are endemic in the country [8]. Concern about ESBL would also account for meropenem (28%) being the most frequently prescribed antibiotic for sepsis, followed by parenteral colistin (10%) and piperacillin–tazobactam (9%).

Cefuroxime (36%), amikacin (10%), and ceftriaxone (8%) were the most frequently used antimicrobials for surgical prophylaxis. Of concern, the majority of patients (77%) who received surgical prophylaxis were treated for more than one day. Only 14% received the single dose of surgical prophylaxis that is recommended for most surgical procedures in international guidelines. The ESAC PPS also reported a high proportion of patients (57.3%) receiving $>$1 day of surgical antimicrobial prophylaxis. In the same study, single-dose preoperative prophylaxis was used only in 25.2% patients [8]. Though the effectiveness of single-dose prophylaxis versus one or two postoperative doses is still controversial, no evidence supports the practice of prolonging the surgical prophylaxis for $>$24 h [9]. Prolonged prophylaxis increases the risks of antimicrobial resistance and side-effects, and is generally unnecessary [9,10]. Thus, this is a crucial quality indicator that needs to be harnessed in the coming years to combat the threat of antimicrobial resistance.

The percentage of multidrug-resistant organisms (MDROs) was calculated using microbiological cultures for patients who received targeted antimicrobial therapy. A total of 77 (18.4%) MRSOs were found. Among the patients receiving at least one antibiotic targeting at least one resistant micro-organism, 22 (5.3%) were ESBL-producing Enterobacteriaceae (77.3% *Klebsiella* spp. and 22.7% of *E. coli*); 16 (3.8%) were carbapenem-resistant Enterobacteriaceae (CRE) (all *Klebsiella* spp.); 11 (2.6%) were ESBL-producing non-fermenting Gram-negative bacteria (72.7% *Acinetobacter baumannii* and 27.3% *Pseudomonas aeruginosa*); and 11 (2.6%) were carbapenem-resistant non-fermenting Gram-negative bacteria. The 2015 ECDC PPS showed a similar AMR pattern as did a previous Indian study [6,8].

The quality indicators for antibiotic use in medical and surgical wards and intensive care units were also assessed in the survey (Table II). Only 42.5% of prescriptions documented

Table II
Summary of quality indicators for antibiotic use

Quality indicators	Medical ward		Surgical ward		ICU	
	No.	%	No.	%	No.	%
Reason for prescribing documented in notes	188	45.5	178	47.3	245	37.9
Guidelines missing	85	20.6	91	24.2	103	15.9
Guideline compliant	167	70.2	142	70	276	79.5
Stop/review date documented	78	18.9	181	48.1	315	48.7

ICU, intensive care unit.

the reason for prescribing antimicrobials in the medical notes, compared with 64% in the ESAC study [8]. The four antibiotic quality indicators that we studied were also included in the Global-PPS 2015, in which 76.9% of antimicrobial prescriptions included reason for treatment, 38.3% prescriptions mentioned stop or review date, antibiotic guidelines were missing for 19.2%, and 77.4% prescriptions were guideline compliant. We suggest that documentation of the reason for prescribing is a key target for quality improvement in India, because it ensures communication of diagnosis and treatment among clinicians and other healthcare providers, thus facilitating all other components of antibiotic stewardship actions [6].

The strengths of our study include the uniformity of data collection, the simplicity of the protocol and data collection templates, data completeness and validation via the Internet-based tool, and the opportunity for real-time educational feedback of results to participating centres (including comparisons with national and regional results) [6].

At the same time, this study was also challenging in terms of controlling the patient case mix, disease incidence, prevalence of different types of infection, variations in resistance levels, institutional factors — all of which may affect and influence antibiotic use patterns, thus prompting caution while interpreting the reported prevalence.

Global PPS has importantly facilitated hospitals to benchmark their prescribing practices, and to devise innovative strategies to improve prescribing practice. The study suggests high levels of antibiotic use across 16 tertiary care and specialized centres within India. The results of the survey underline the need for antibiotic stewardship in order to promote rational and evidence-based practice, and they should also help identify targets for quality improvement (focusing on documentation of the reason for prescribing antibiotics in the medical records).

Acknowledgements

We thank all healthcare team members of the 16 centres for their contribution towards the survey and would like to acknowledge the support provided by Dr K. Walia, Senior Scientist from the Indian Council of Medical Research.

Conflict of interest statement
None declared.

Funding source
bioMérieux.

Appendices A and B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2019.05.014.

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