Investigation of Queries Related to Antimicrobial Agents Use in a Tertiary Hospital from 2015 to 2018

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Authors’ contributions

This work was carried out in collaboration among all authors. Authors AUA, A. A. Alfaifi, NJA and A. A. Albassam designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AHAN, MSA and AKA managed the literature searches and managed the analyses of the study. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2020/v32i3330950
Editor(s): (1) Dr. Arun Singh, Rohilkhand Medical College & Hospital, India.
Reviewers: (1) Tzasna Hernandez, UBIPRO, National Autonomous University of Mexico, Mexico. (2) P. Rama Bhat, Alva’s College, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/62809

Received 12 September 2020
Accepted 18 November 2020
Published 09 December 2020

ABSTRACT

Aim: This study compares factors associated with requests for antimicrobial agents versus those for other types of treatment, contrasting the requests of pharmacists versus those of other healthcare staff related to antimicrobial agents.

Methods: A retrospective cross-sectional study was conducted for all requests received from January 1, 2015, to December 31, 2018. A series of chi-squared tests was used to analyze the relationship between different categories. All data analyses were conducted using the R statistical computing language.

Results: In total, 2,423 requests were received from 2015 to 2018, of which antimicrobial agents accounted for 21.67%. The highest percentages of antimicrobial requests by pharmacists were related to administration and dosage forms, pregnancy and lactation, and stability. A majority of the requests were answered using tertiary resources. The most-requested information regarding antimicrobial agents was related to clindamycin.

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Conclusion: Because many requests pertaining to antimicrobial agents were made, as a proportion of total drug and poison information centre requests, from 2015 to 2018, pharmacists should maintain and indeed expand their active role to combat antibiotic resistance.

Keywords: Drug information requests; antimicrobial agents; antibiotics; medical resources.

1. INTRODUCTION

Antimicrobial resistance (AMR) results from modifications undergone by microorganisms exposed to antimicrobial drugs, including antibiotics. Superbugs, or microorganisms that produce antimicrobial resistance, can increase the risk of spreading infection so that drugs become ineffective and infections continue in the body [1]. As a result, the risk of AMR, including multidrug resistance (MDR), in health-care facilities and communities is increasing [2].

According to the World Health Organization (WHO), 3.7% of new cases and 20% of previously treated cases are prone to MDR-TB globally [3]. In the United States, at least 2 million patients are infected with antibiotic-resistant bacteria, as a result of which 23,000 people die [4]. In Europe, more than 25,000 patients die annually as a result of infections caused by resistant bacteria, for an estimated $1.6 billion in added health-care costs and productivity losses. Indeed, cumulative losses in the EU due to AMR could reach $2.9 trillion by 2050 [5].

Saudi Arabia receives various local reports of antibiotic resistance or hospital-associated infection. Al-Obed and colleagues found a major decrease in the susceptibility of A. baumannii to meropenem and imipenem, from 64–61.2% in 2006 to 8.3–11% in 2012 [6]. Halwani and colleagues explored penicillin-resistant strains of Streptococcus pneumoniae in King Fahd Hospital, Al Baha [7]. They detected, on average, 70% resistance, with most S. pneumoniae isolated from respiratory specimens [7]. A retrospective study conducted from 2004 to 2009 to screen gram-negative isolates from adult patients in an intensive care unit in King Fahad National Guard Hospital revealed a significant decrease in antibiotic susceptibility in various microorganisms [8]. More than 40% decline was detected in baumannii’s susceptibility to imipenem, as well as a more than 40% decline in S. marcescens’s susceptibility to cefotaxime and ceftazidime [8].

Antibiotic resistance has been reported to increase the risk of poor clinical outcomes and death [6]. Patients infected with antibiotic-resistant bacteria exhibit higher levels of health-care use than do patients infected with nonresistant strains of bacteria [9]. Accordingly, action should be taken at all levels to lessen the influence, and limit the spread, of such resistance. Without decisive action, a post-antibiotic age could ensue in which antibiotics no longer work on minor and common infections.

Antimicrobial resistance can be overcome in part through the efforts of drug and poison information centers (DPICs) in hospitals. One of the main elements of hospital antibiotic stewardship programs is to assign a pharmacist manager responsible for enhancing antimicrobial use [10]. Pharmacists can advocate rational use of antimicrobial agents while gathering information on their associated incidence of poisoning and drug side effects [11]. As increasing numbers of medications are approved for clinical use, health-care professionals need assistance determining dosages, uses, and other medication-related issues. However, because physicians and pharmacists have limited access to information about drugs and chemicals, drug and poison information centers work to provide accurate and timely drug information to those who urgently need it [12]. Shadniaa and colleagues analyzed more than 9,500 telephone calls received by the Loghman-Hakim drug and poison center and found that the second most common topic of calls, after antidepressants, was antimicrobial drugs [13].

It has been shown that AMR is as prevalent as it is because prescribers’ lack of knowledge and experience lead to misuse and abuse of antimicrobial agents [14]. Glasgow and colleagues found that more than 25% did not know whether AMR was a substantial issue where they practiced, with most prescribers believing that it was not. Nevertheless, pharmacists held strong positions on the AMR issue [15]. This study thus offered insights into the role of pharmacists in hospitals’ drug and poison information centers in overcoming antibiotic use and resistance. Accordingly, the aim of the present study is to compare factors associated with requests related to antimicrobial agents versus those for other types of treatment,
as well as to contrast requests from pharmacists to other health-care staff related to antimicrobial agents.

2. MATERIALS AND METHODS

A retrospective cross-sectional study was conducted for all requests received from January 1, 2015, to December 31, 2018, in the Drug and Poison Information Center at Security Forces Hospital (SFH), Riyadh, Saudi Arabia. SFH, a tertiary care facility with over 508 beds, provides care for Ministry of Interior employees and their dependents [16].

Two independent pharmacists were assigned to screen all drug information requests, then create the dataset. Each phone call was treated as a unit of analysis, and for each unit a set of variables was created: type of request (related to antimicrobial), data of the request, requester profession, and request class. Antimicrobial agents were classified by WHO definition as antibacterial, antiviral, antifungal, or antiparasitic [17]. Requester profession was categorized by registration in the hospital system, which aligned with the Saudi Commission for Health Specialties [18].

Further analysis was conducted by two pharmacists for all requests flagged as “antimicrobial agents” to validate the request class and create sets of variables: type of antimicrobial, medication class, medication name, and type of source used to obtain answers. Micromedex was used to aid in creating the type, class, and name of each medication [19]. Drug information sources used to generate responses for requests were categorized into three groups: primary, secondary, and tertiary [20].

A series of chi-squared tests was used to analyse the relationship between different categories. These variables were created to compare the proportions of subjects in both groups who requested the information—that is, pharmacists versus other HCPs, as well as antimicrobial versus other treatment types. All data analyses were conducted using the R statistical computing language.

3. RESULTS

A total of 2,423 requests were received from 2015 to 2018, of which 68.09% came from pharmacists and 31.91% from other health-care providers. Antimicrobial agents accounted for 21.67% of total requests. A chi-squared test of independence was performed to examine the relation between type of antimicrobial agent and request class. The relation between these variables was significant, $\chi^2 (6, N = 2,423) = 34.80, p < .0001$.

Table 1 compares antimicrobial requests with other treatment requests, exploring the relationship between treatment type and request year. Together, 2016 and 2017 accounted for 58.35% of requests. The range of antimicrobial requests varied by year, with the highest percentage seen in 2015 (23.04%) and the least in 2016 (20.34%). Even so, the relationship between treatment type and request year was not significant $\chi^2 (3, N = 2,423) = 1.58, p = 0.6637$. Of questions pertaining to antimicrobials, most requests were for antibiotics (77.67%), followed by antivirals (13.17%) and then other antimicrobials (9.16%). The relationship between type of antimicrobial and type of profession was significant, $\chi^2 (2, N = 524) = 10.20, p = 0.0061$.

Table 2 compares pharmacists’ requests with other health-care providers’, mainly physicians and nurses. For request class, the highest percentages of antimicrobial requests made by pharmacists were related to administration and dosage forms, pregnancy and lactation, and stability, whereas for other health-care staff they were related to availability and supply, side effects, and drug interactions. The relation between these request classes and profession types was significant, $\chi^2 (6, N = 524) = 52.71, p < .0001$. The majority of the requests were answered using tertiary resources (84.93%), with primary and secondary resources representing the remainder (15.07%). The correlation between reference type and profession type was significant, $\chi^2 (1, N = 524) = 11.40, p = 0.0007$.

Table 3 lists the most requested (top 10) antimicrobial agents by generic name. The majority of these medications (nine) were antibiotics, and only one was antifungal (fluconazole). Two macrolide agents, clindamycin and azithromycin, were among the top three requested antibiotics. The top requested generic treatments were clindamycin, Augmentin, azithromycin, ciprofloxacin, metronidazole, fluconazole, doxycycline, cefuroxime, vancomycin, and nitrofurantoin.
Table 1. Comparison between antimicrobial requests versus other treatment requests

| Variable                  | Type of Treatment | Total | P-Value |
|---------------------------|-------------------|-------|---------|
| **Requester Profession**  |                   |       |         |
| Pharmacist                | 369 (22.36%)      | 1,281 (77.64%) | 1,650   |
| Non-pharmacist            | 156 (20.18%)      | 617 (79.82%)  | 773     |
| **Request Class**         |                   |       |         |
| Administration and dosage| 385 (23.69%)      | 1,240 (76.31%) | 1,625   |
| Pregnancy and lactation   | 45 (27.11%)       | 121 (72.89%)  | 166     |
| Drug interaction          | 33 (25.00%)       | 99 (75.00%)   | 132     |
| Stability                 | 9 (10.11%)        | 80 (89.89%)   | 89      |
| Availability and supply   | 18 (10.11%)       | 160 (89.89%)  | 178     |
| Side effect               | 11 (15.94%)       | 58 (84.06%)   | 69      |
| Other                     | 24 (14.63%)       | 140 (85.37%)  | 164     |
| **Year**                  |                   |       |         |
| 2015                      | 144 (23.04%)      | 481 (76.96%)  | 625     |
| 2016                      | 144 (20.34%)      | 564 (79.66%)  | 708     |
| 2017                      | 156 (22.10%)      | 550 (77.90%)  | 706     |
| 2018                      | 81 (21.09%)       | 303 (78.91%)  | 384     |

Table 2. Comparison between pharmacist requests versus other health-care providers

| Variable                  | Question Source | Total | P-Value |
|---------------------------|-----------------|-------|---------|
| **Type of Antimicrobial** |                 |       | 0.0061  |
| Antibiotic                | 121 (29.73%)    | 286 (70.27%) | 407     |
| Antiviral                 | 29 (42.03%)     | 40 (57.97%)  | 69      |
| Others                    | 7 (14.58%)      | 41 (85.42%)  | 48      |
| **Request Class**         |                 |       | <.0001  |
| Administration and dosage| 87 (22.72%)     | 296 (77.28%) | 383     |
| Pregnancy and lactation   | 15 (33.33%)     | 30 (66.67%)  | 45      |
| Drug interaction          | 16 (48.48%)     | 17 (51.52%)  | 33      |
| Stability                 | 3 (33.33%)      | 6 (66.67%)   | 9       |
| Availability and supply   | 15 (78.95%)     | 4 (21.05%)   | 19      |
| Side effect               | 7 (70.00%)      | 3 (30.00%)   | 10      |
| Others                    | 14 (56.00%)     | 11 (44.00%)  | 25      |
| **Reference Type**        |                 |       | 0.0007  |
| Primary and secondary     | 11 (13.92%)     | 68 (86.08%)  | 79      |
| Tertiary                  | 146 (32.81%)    | 299 (67.19%) | 445     |

Table 3. Antimicrobial agents subject to the most requests from DPIC

| Name of Antimicrobial Agent | Frequency (%) |
|-----------------------------|---------------|
| Clindamycin                 | 39 (7.44%)    |
| Augmentin                   | 36 (6.87%)    |
| Azithromycin                | 30 (5.73%)    |
| Ciprofloxacin               | 26 (4.96%)    |
| Metronidazole               | 24 (4.58%)    |
| Fluconazole                 | 21 (4.01%)    |
| Doxycycline                 | 20 (3.82%)    |
| Cefuroxime                  | 20 (3.82%)    |
| Vancomycin                  | 19 (3.63%)    |
| Nitrofurantoin              | 18 (3.44%)    |

4. DISCUSSION

This comprehensive study was conducted to assess health practitioners' requests related to antimicrobial medications. About 21% of requests made to the DPIC at Security Forces Hospital, Riyadh, Saudi Arabia, were related to antimicrobial agents, making them the primary reason for contacting DPIC. A previous study analyzing inquiries made to drug information centers from 2013 to 2015 found that questions relating to antimicrobial agents accounted for 20% of questions received [21]. These results validate the importance of health-care training regarding the use of antimicrobial...
agents to combat resistance at multiple levels [22].

The number of calls increased from 2015 to 2017, followed by a nearly 50% decline in 2018—an effect perhaps attributable to the presence of the new Saudi Arabia Ministry of Health (MOH), a point-to-point communications center. This service center, established in 2018, is responsible for handling drug inquiries from HCPs and the public, as well as for handling and updating the MOH’s drug list, so that it essentially functions as a nationwide drug information center ensuring safe and effective use of medicine [23].

More than 73% of questions asked of the SFHDPIC about antimicrobial agents were related to administration and dosage of antimicrobial agents, indicating that HCPs seek to achieve the best regimen and dose for their patients—it being well established that treating patients with low levels of antibiotics can lead to high levels of AMR [24]. Likewise, the second most common topic of calls was pregnancy and lactation, indicating that HCPs were trying to obtain the latest information when prescribing antimicrobials to their patients—as prescribing medications to lactating and pregnant women has certain inherent risks, and because adequate and well-controlled clinical trials are lacking in the medical literature with which to ascertain the efficacy and safety of antimicrobials during pregnancy [25].

This study found high levels of variability among health-care providers in their requesting of information. Pharmacists contacted DPIC about AMR more than all other professions combined, as well as accounting for the majority of resource types used to answer requests, whether tertiary, secondary, or primary. However, the percentage of increased greatly, from 67% using tertiary resources to 86% using primary and secondary resources. Accordingly, the relation between profession and resource type was significant, with complex requests mainly originating with pharmacists. It has been established that pharmacists are more educated, trained, and expert in antibiotic use in community and hospital settings [26,27]. Notably, then, they are more willing to contact DPIC to ensure that they are following applicable guidelines.

Clindamycin was the antibiotic most inquired about, whereas vancomycin ranked ninth in inquiries pertaining to antimicrobial agents. Although this contradicted the previous findings of Chi-Lien Hou et al., who reported that vancomycin was the single drug most inquired about at a medical center in Taiwan [21], this is not surprising, considering that vancomycin resistance is more prevalent in developed countries [28], whereas Saudi Arabia experiences greater prevalence of clindamycin resistance instead [29,30]. These facts could explain variations in most requested antimicrobial agents while reaffirming that resistance drives the majority of drug information center inquiries.

5. CONCLUSION

A substantial number of requests pertaining to antimicrobial agents were included in total DPIC requests from 2015 to 2018. Pharmacists were associated with higher percentages of complex questions whose answering required extensive resources, indicating that pharmacists should continue and indeed expand their active role to combat antibiotic resistance.

CONSENT

As per international standard or university standard, respondents’ written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Institutional Review Board (IRB) approval was obtained in July 2019 from the research committee of Security Forces Hospital, which is constituted and functions in accordance with the National Committee of Bio Ethics (NCBE), under IRB number 19-357-55.

ACKNOWLEDGEMENT

This Publication was supported by the Deanship of Scientific Research at Prince Sattam bin Abdulaziz University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/62809