

Knowledge, attitude and practice of clinicians about antimicrobial stewardship and resistance among hospitals of Pakistan: A multicenter cross-sectional study

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Abstract

Considering that antimicrobial resistance (AMR) is a global challenge, there is a dire need to gauge the knowledge, attitude, and practice (KAP) of clinicians in endemic countries. The aim of the current multicenter, cross-sectional study was to highlight the knowledge, aptitude and practice gaps in antimicrobial (AM) stewardship and AMR among practicing doctors working in public tertiary care teaching hospitals of Lahore, Pakistan. A KAP survey, based on a self-administered questionnaire containing 45 questions, was conducted among 336 clinicians practicing in 6 randomly selected hospitals of Lahore, Pakistan. Overall, 92% of the clinicians considered AMR as a worldwide problem but only 66% disagreed that cold and flu symptoms require antibiotics. Moreover, around 68% doctors felt confident about their practice in AM but still 96% felt need to get more knowledge about AM. Need to establish courses on rational antibiotic use was demanded by 84% of participants. The main contributing factors considered for AMR by the doctors included excessive AM usage in medical profession (87.1%) and multiple antibiotics per prescription (76.4%). Pharmacologically, AM spectrum was accurately chosen by 1.4% (ampicillin), 0.003% (erythromycin) and 0% (levofloxacin). Clinically, a more than 50% of clinicians used miscellaneous AM for empirical therapy of respiratory tract infection and cholecystitis. The data was analyzed using Statistical Package for Social Sciences (SPSS) version 25. The knowledge of clinicians is relatively poor in AM spectrum and drugs of choice for certain infections. However, they know about their short comings with positive approach towards improvement.

Introduction

Although there were significant advances in antimicrobial therapy in 1980s as the third-generation cephalosporin and new fluoroquinolones proved to be highly effective. The widespread usage of these newly developed drugs soon gave rise to a new problem. A decade down the line, clinicians started to see persistent infections despite the antibiotic regimens. Newer strains of multi-drug resistant staphylococci, enterococci and streptococcus bacteria were identified.(Levy 1998, Okeke, Laxminarayan et al. 2005, Cosgrove 2006, Organization 2012) With emerging antimicrobial resistance (AMR), there is concordant rise in the morbidity and mortality ratios. Accompanying the high mortality and morbidity was the economic stress this problem had on the health care sector in low-income countries. (Organization 2012) Factors responsible for AMR in the third world countries include over-prescribing, unnecessary prescribing, incomplete treatment course, self-medication and insufficient infection control measures to prevent spread of resistant bacteria both in the community and the hospital.(Okeke 2010, Sosa, Byarugaba et al. 2010) The first step to deal with AMR is to educate the related staff about the over expanding AMR dilemma.(Dellit, Owens et al. 2007, Pulcini, Cua et al. 2007) This knowledge has led USA, France and Scotland to immediately develop a national recommendations program to improve antibiotic stewardship in their countries.(Nathwani 2006, Dellit, Owens et al. 2007, Pulcini, Cua et al. 2007) In certain studies, it is known that the misuse of antibiotics by general population increases the chance of getting infected with the resistant strains of bacteria, yielding higher morbidity and mortality.(Cabana, Rand et al. 1999, Woodford and Livermore 2009, Costelloe, Metcalfe et al. 2010) Meanwhile, the best

approach to contain AMR is to minimize the antimicrobial usage and it can be achieved by changes in prescribing behavior.(Wester, Durairaj et al. 2002, Giblin, Sinkowitz-Cochran et al. 2004, Srinivasan, Song et al. 2004, Guerra, Pereira et al. 2007, García, Llamocca et al. 2011, Pulcini, Williams et al. 2011) Factors thriving prescribing behavior of medical doctors can be analyzed by evidence focused questionnaire such as knowledge, attitude and practice (KAP) surveys.

In addition, the available studies have all been in Europe, U.S. China, Brazil, and Peru but few studies were done in Pakistan.(Wester, Durairaj et al. 2002, Giblin, Sinkowitz-Cochran et al. 2004, García, Llamocca et al. 2011, Faizullah, Nisar-ur-Rahman et al. 2017, Shahid, Iftikhar et al. 2017, Ahmed, Bhimani et al. 2020) Therefore, we conducted a KAP-survey about antimicrobial usage and antimicrobial resistance among public tertiary care teaching hospitals of Lahore, Pakistan.

Methodology

It was a cross-sectional study in which a self-administered questionnaire was distributed among physicians at the postgraduate trainee level and faculty in six randomly selected tertiary care teaching hospitals of Lahore, Pakistan. The variables encountered were knowledge of doctors regarding antimicrobial usage and its resistance, their attitude towards antimicrobial usage and resistance, and their practice concerning both. The inclusion criteria included clinicians working in medicine, surgery, and their allied departments. Psychiatrists, radiologists and basic sciences doctors were excluded. The questionnaire was distributed on-site during working hours in hard copy along with the option of filling it digitally.

The questionnaire was developed in consultation with a group of experts on questionnaire design and infectious diseases, and after searching the literature for comparable studies.(Wester, Durairaj et al. 2002, Srinivasan, Song et al. 2004, Guerra, Pereira et al. 2007) Before we finalized the questionnaire, it was reviewed by a panel of clinical experts of Shaikh Zayed Post-Graduate Medical Complex, Lahore, Pakistan. The questionnaire enquired the participants' awareness regarding the recent scope of antimicrobial resistance (15 questions), the clinical attitude contributing to the above-mentioned fact inputs (5 questions), factors influencing confidence regarding usage and prescription of AM and AMR (6 questions), knowledge regarding contributing factors of AMR (7 questions) and basic knowledge about the clinical indications, spectrum, administration and pharmacology of antimicrobials (12 questions). The questions used a 4 or 5-point Likert scale (which included answers ranging from "strongly agree" to "strongly disagree", from "very confident" to "not confident" and from "always" to "never"). The anonymous nature of questionnaire and prior consent form from all clinicians addressed ethical issues. This research was in accordance with principle 3 and 4 of World Medical Association's declaration of Helsinki. The questionnaire was submitted in a pilot test to 34 participants to check comprehension and clarity of the questions.

Randomized selection of tertiary care teaching hospitals of Lahore by using lottery method was done which made us to select Ganga Ram Hospital, Jinnah Hospital, Services Hospital, Mayo Hospital, Sheikh

Zayed Hospital and General Hospital. Sample size was calculated using www.epitool.ausvet.com with estimated true proportion 0.5 with confidence level of 95% and desired precision of 0.05, the population size was calculated to be 2614 doctors. The doctors were contacted after consultation with administrators/ medical superintendents of respective hospitals among the 6 hospitals, and the calculated sample size was 336. It was predefined that a questionnaire was to be considered valid for analysis if 90% of questions were answered. The data was analyzed using IBS SPSS software version 25 (SPSS Inc., Chicago, IL, USA)

Results

All participants had at least a Bachelor of Medicine and Bachelor of Surgery (MBBS) degree with mean age of 31 years. Of the total, 336 filled questioners, 84.5% (284) met the selection criteria. Among those, 34.5% were males and 25.7% were faculty members (Table 1). In our study (Fig. 1), 92% of the clinicians considered AMR as a worldwide problem but only 66% disagreed that cold and flu symptoms require antibiotics. Though, around 68% doctors felt confident about their knowledge and practice in the antibiotic prescription but still 96% felt necessary to get more knowledge about AM. Along with that, 20% believed AM prescription would not cause damage. Furthermore, 78% doctors blamed that poor-quality antibiotics made them ineffective, while 35% believed efficacy would be better with newer costly antibiotics. Furthermore, 19% thought patients' demand contributed to over-prescription while 17% considered over-prescription better than under-prescription in infected patients and 37% agreed antimicrobials should be available over the counter. Moreover, 69% believed AMR is not a problem in their clinical settings along with 84% demanded need to establish courses on rational antibiotic use and to carry out large scale antibiotic awareness (39%)

According to the study (Fig. 2A), antibiotics were being selected confidently by 75.4% doctors and more than 81% felt confident while planning duration of AM treatment however 74.3% felt confident while stopping treatment. More than 75% of the respondents felt confident while selecting correct dose, duration of administration and using combination therapy. Almost 80% were also confident that they could choose between intravenous and oral routes correctly.

The factors which were regarded as being important causes of antibiotic resistance included: multiple antibiotics per prescription (76.4%) and excessive use of AM in daily life (87.1%). The factors most frequently identified as less important included: prescribing too many broad-spectrum antibiotics (61.7%), prescribing low dose antibiotics (60.5%), longer duration of AM usage (66.2%) and poor hand hygiene (54.9%). The factor which was regarded as least important was paying too much attention to advertising (36.3%) (Fig. 2B).

65% of doctors felt mostly confident about prescribing antibiotics while 40% considered sometimes about AMR while prescribing. Half of the respondents agreed that doctors sometimes got influenced by multinational companies while approximately 1/4th of the doctor community belonged to the class who believed it occurred more often. 50% of doctors sometimes, and 30% most of the times reviewed their

choice for antibiotic usage with their senior colleagues and 11% of the times mostly and 71% sometimes suggested a different antibiotic (Fig. 2C).

Knowledge about the empiric therapy of various common infections was inquired (Fig. 3). For urinary tract infection (uncomplicated), around one half of the doctors prescribed ciprofloxacin, while levofloxacin and TMP-SMZ were written by 11.4% and 5.6% respectively as first line treatment. Upper respiratory tract infection was being managed supportively by only 3.9% of clinicians as per world health organization (WHO) recommendations while one fourth were managing via amoxicillin and around 10% were being treated by levofloxacin and azithromycin cumulatively. Shockingly, more than 70% were prescribing miscellaneous drugs. In clinical practice, doctors considered ciprofloxacin and metronidazole in around 31% and 40% of their prescriptions respectively as first line treatment of gastroenteritis while only 11% decided to manage it conservatively. First line of choice for community acquired pneumonia by approximately 13 doctors was amoxicillin, levofloxacin and ceftriaxone individually, azithromycin was prescribed by 7% of them and more than 50% of prescriptions were contributed by miscellaneous drugs. Most of the clinicians (50%) prescribed miscellaneous drugs as first line antibiotic while others chose different drugs for treatment of cellulites that include amoxicillin (9.6%) and ceftriaxone (7.4%). Also 26.9% clinicians chose drugs other than these for the said purpose. As far as cholecystitis was concerned, majority disputed on the first line antimicrobial by choosing miscellaneous drugs (57%), all different agents being prescribed for that.

Knowledge about the antimicrobial spectrum was also evaluated (Fig. 4). 1.4% of the clinicians chose correct spectrum of Ampicillin.(Rafailidis, Ioannidou et al. 2007) However, 88.3% were inclined towards gram positive cocci, 39.2% considered it to be active against gram positive bacilli, 31.8% believed it to be active against gram negative cocci, 14.3% suggested it as a preferred treatment for gram-negative bacilli and 2.6%, 10% and 3.3% marked anaerobes, spirochetes, and atypical bacteria respectively. Amazingly, the correct antimicrobial spectrum of Metronidazole(Freeman, Klutman et al. 1997) was selected by 61.6%. However, 85% of doctors do know that it is effective against anaerobes while 13.3% considered its coverage for gram-positive cocci and other lesser percentages of doctors considered it to be effective against other organisms. Astonishingly, none of the clinicians were able to identify the correct antimicrobial spectrum of Levofloxacin.(Zhanel, Fontaine et al. 2006, Anderson and Perry 2008) On the better side, greater than half of doctors knew its effectiveness against gram positive cocci, more than 1/3rd considered it effective against gram positive bacilli and gram-negative rods along with that 20% correctly identified it to be effective against atypical bacteria. However, around 40% of the doctor community also thought it to be effective against gram-negative cocci. Only one doctor (0.003%) came up with the correct antimicrobial spectrum for Erythromycin (Lartey, Nellans et al. 1994, Zhanel, Dueck et al. 2001) but 68.2% of the doctors considered its coverage against gram positive cocci to be true. Almost 25–35% of the doctors contemplated its effectiveness against, gram negative bacilli, gram negative cocci, gram positive bacilli and atypical bacteria. Around 5.9% considered it to be effective against spirochetes but 6.8% believed it also acted on anaerobes. 0.4% picked correct spectrum of vancomycin, 77.4% chosen gram positive cocci while gram negative cocci and gram positive bacilli were chosen by around 33% clinicians.(Wilhelm and Estes 1999, Marsot, Boulamery et al. 2012) Anaerobes, spirochetes

and atypical were marked by less than 10% of doctors. 2.8% of the doctors opted correct spectrum of Ceftriaxone.(Cleeland and Squires 1984, Lamb, Ormrod et al. 2002) 53.9% selected gram positive cocci as right option whereas 66.3% handpicked gram negative cocci. Gram positive bacilli were nominated as the correct option by 29.1% while 39.1% saw gram negative bacilli as correct option. Anaerobes (9.4%), spirochetes (11.3%) and atypical (10.7%) were marked.

Discussion

This survey demonstrated the knowledge, attitude, and practices of doctors regarding antimicrobial resistance in six large public teaching hospitals in Lahore. From the study, it was evident that the knowledge about AMs resistance, their misuse, and the concern regarding their emerging resistance problem worldwide was apt. But despite all this, on ground realities were quite astonishing as most of the physicians were using AMs even for mild upper respiratory tract infections. Moreover, their attitude for prescribing multiple antibiotics per prescription was also questionable. Majority of the doctors' knowledge pertaining to AM spectrum and empirical treatment for certain infections was not up-to the mark. This shows that special attention should be given to this matter and appropriate interventions must be used to improve the knowledge of doctors in this area. It was evident from the study that 91.9% participants considered AMR to be uprising concern, yet AMR was almost completely ignored in their own practice. Majority agreed on the fact that the main reason for such growing resistance is the daily frequent use of AM. A small ray of sunshine was seen that a number of newer doctors were seen seeking help from their experienced colleagues when prescribing, irrespective of their specialization (department) so that the appropriate antibiotic could be given to avoid resistance. However, 40% of participants responded that they did not consult their peers. 19.4% of the participants shed light on the issue that overuse of AMs is a consequence of patient's demand and it is due to their limited understanding of the fact that antibiotics aren't the curative medication for every disease and excessive use has side effects. They also need to know that these drugs have no effect on viral infections. These results were in contrast to a study done in a hospital of Peru that showed patient's pressure to prescribing antimicrobials was considered as a major contributing factor (72%) to AM overuse in community. Similarly, a study done in Alexandria university teaching hospital also concluded that antibiotic prescription by physician was influenced by patient's demands (78.5%) and socioeconomic status (76.3%). So, we have concluded that awareness of public through community-targeted media is immensely important. More than half of the participants agreed that AMs in their hospitals are of poor quality. Although we have not explored in detail the definition of "poor" quality. The two main reasons for such substandard quality of medicines include the counterfeit drugs detected in Lahore. Secondly, the use of generic drugs is frequently perceived to be less effective. This affects the physician ability to treat a disease effectively as well as the doctor-patient relationship. The Pakistan Ministry of Health should take some serious action as it is an important issue which directly relates to patient health. The availability of standardized antibiotics should be made possible so that the treatment won't be compromised.

To our best knowledge this is the first multicenter cross-sectional study assessing knowledge, attitude and practice of antimicrobials and antimicrobial resistance of clinicians in Lahore, Pakistan. A uni-center

study conducted in Services hospital, Pakistan, also concluded that antibiotic overuse has become a major problem as 70% of physicians were prescribing more than one antibiotic per day and 80% of the physicians reviewed their decision to prescribe antibiotic by discussing with an experienced colleague that showed that the knowledge of freshly graduated physicians regarding antibiotic prescription, was not up to the mark. Similarly, a study conducted among healthcare workers in Iran showed 88% agreed on establishment of local guidelines and 94% believed that education regarding antibiotics can help reduce AMR.

Educational and awareness programs regarding the vigilant use of antimicrobials and AMR should be conducted on regular basis. Mandatory continuing medical education courses should be attended by the healthcare professionals to explain their role in limiting the misuse of antimicrobials and emerging AMR. Moreover, active educational techniques including clinical scenarios that simulate real clinical settings, objective centered clinical examinations, awareness campaigns, and interactive learning workshops should be regularly conducted (Yang, Wu et al. 2016) Future studies from distant, primary and secondary health centers are recommended.

The anonymous nature of questionnaire and voluntary involvement provided reliable answers with no social pressure. Despite the strengths, the study also has some potential limitations. First, a majority of the samples (74.3%) was postgraduate trainees in their respective departments. Additionally, a stringent criterion was used to access the knowledge of antimicrobial spectrum which may not be clinically relevant. Another limitation of the study was that the participants from non-teaching hospitals and rural/basic health centers were not interviewed. Moreover, in KAP-survey sometimes the physicians get socially pressurized and give more socially acceptable answers rather than expressing their true opinions. Therefore, to reduce this potential bias, incognito participation was made certain and the case-based questions about AM prescription were composed. Another problem was that consultants working in hospitals did not give due attention to the lengthy questionnaire so it would be apt to say that further studies should be done to access the knowledge, attitudes and practice about antimicrobial use among physicians from community centers. As this study was conducted in six large, public, tertiary-level teaching hospitals, and significant number of qualified prescribing doctors were a part of this, we are positive that the outcomes will be applicable to other public hospitals in Pakistan. Future studies from peripheral health centers are recommended.

Conclusion

The present KAP-survey has generated information about the knowledge, prescribing attitudes, and practices of medical doctors among all public tertiary care teaching hospitals of Lahore, Pakistan. It highlighted the areas that need improvement to prevent the AMR. The knowledge of clinicians is relatively poor when it comes to drug spectrums and drugs of choice for certain infections. However, the clinicians know about their short comings and they have a positive approach towards professional development.

Declarations

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Authors Contributions: SoA, ShA, MoA and MAI drafted the first draft and all authors participated in writing subsequent drafts. SoA, MoA, MAI and ZA, AbA, contributed in collecting data and its interpretation. ZA, SoA, MAI and MKA drafted the figures and the Table. AH, QaS, MA, and MI supervised and edited the follow up drafts. All authors approved the final manuscript.

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Data Availability: The data used during the current study is available from the corresponding authors on reasonable request.

Competing Interest: Authors declare no competing interest and all the authors have seen and agreed to the submission of this paper.

Ethical Approval: Ethical approval was taken from institutional review board of Shaikh Zayed Post-Graduate Medical Institute, Lahore.

Consent to Participate: Written informed consent was taken from participants for data collection and maintaining confidentiality.

Consent to Publish: Not applicable.

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Tables

Table 1: Demographic Characteristics of Participants		Number (percentage)
Gender	Male	98 (34.5)
	Female	186 (65.5)
Years of experience	≤5	198(69.72)
	5-10	37(13.03)
	≥10	49(17.25)
Age	≥40	47(16.55)
	<40	237 (83.45)
Hospital	SZH	58 (20.4)
	JHL	57 (20.1)
	Mayo	60 (21.1)
	General	55 (19.4)
	SIMS	54 (19.0)
Position	Post Graduate Trainees	211 (74.3)
	Medical Officer	30 (10.6)
	Assistant Professor	18(6.3)
	Associate Professor	11 (3.9)
	Professor	14(4.9)
Department	Medicine	82 (28.9)
	Medicine Allied	93 (32.7)
	Surgery	47 (16.5)
	Surgery Allied	62 (21.8)

Figures

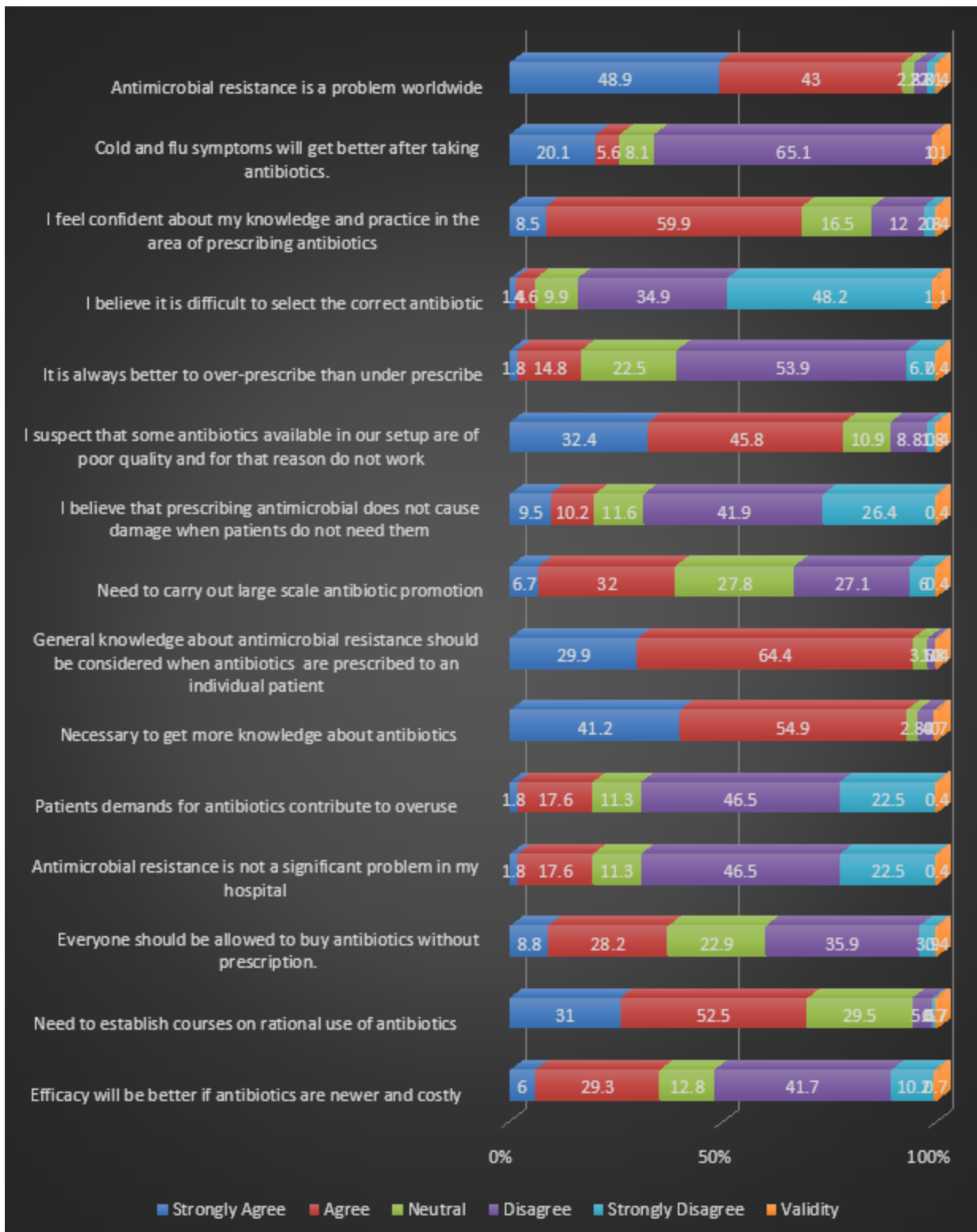


Figure 1

Awareness of the scope of AMR among 284 participants (data in the graph represents percentages)

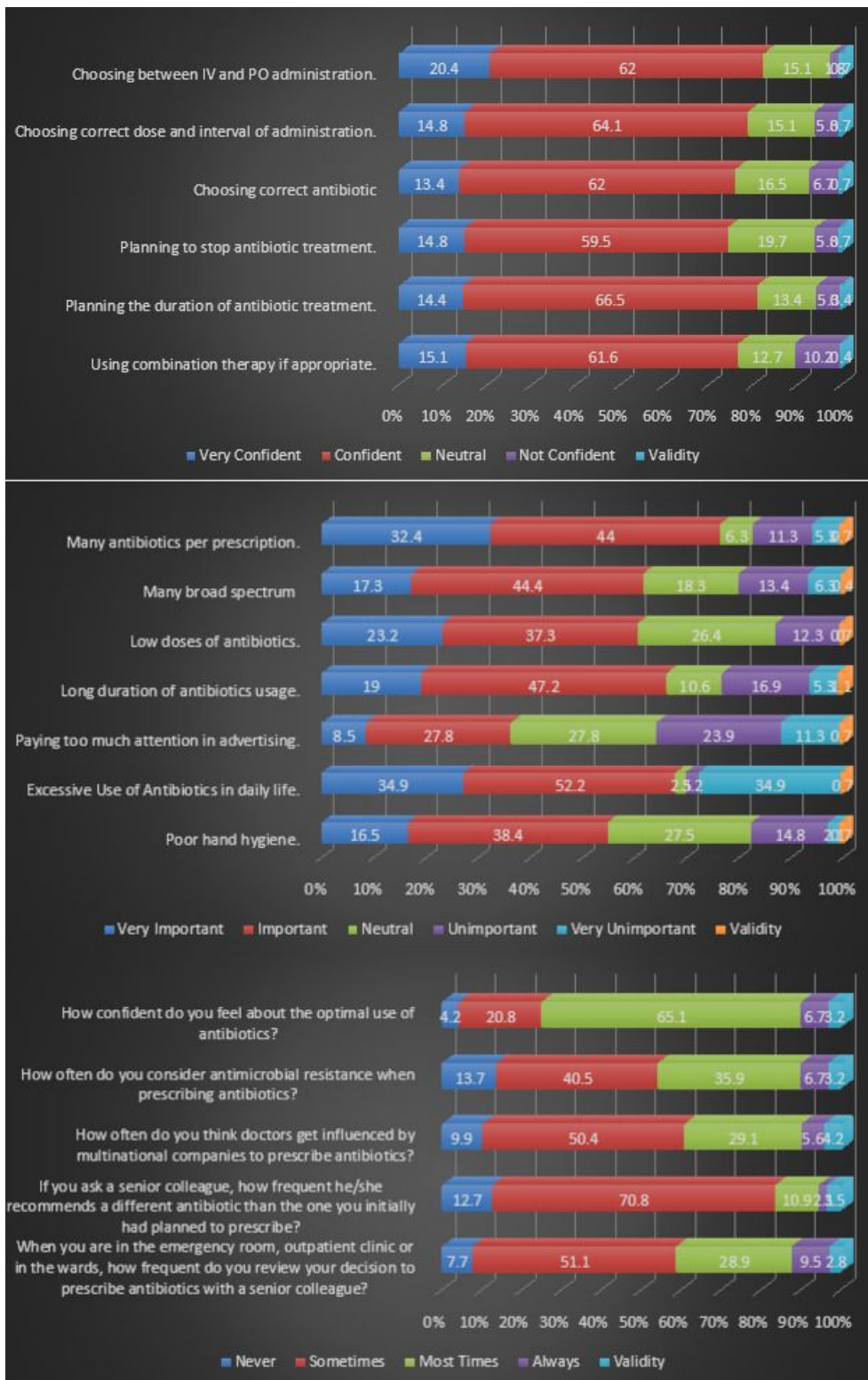


Figure 2

(A): Factors influencing the clinicians' knowledge leading to AMR. Data represent percentages among 284 participants. (B): Factors influencing the clinicians' practice leading to AMR. Data represent percentages among 284 participants. (C) Factors influencing the clinicians' attitude leading to AMR. Data represent percentages among 284 participants

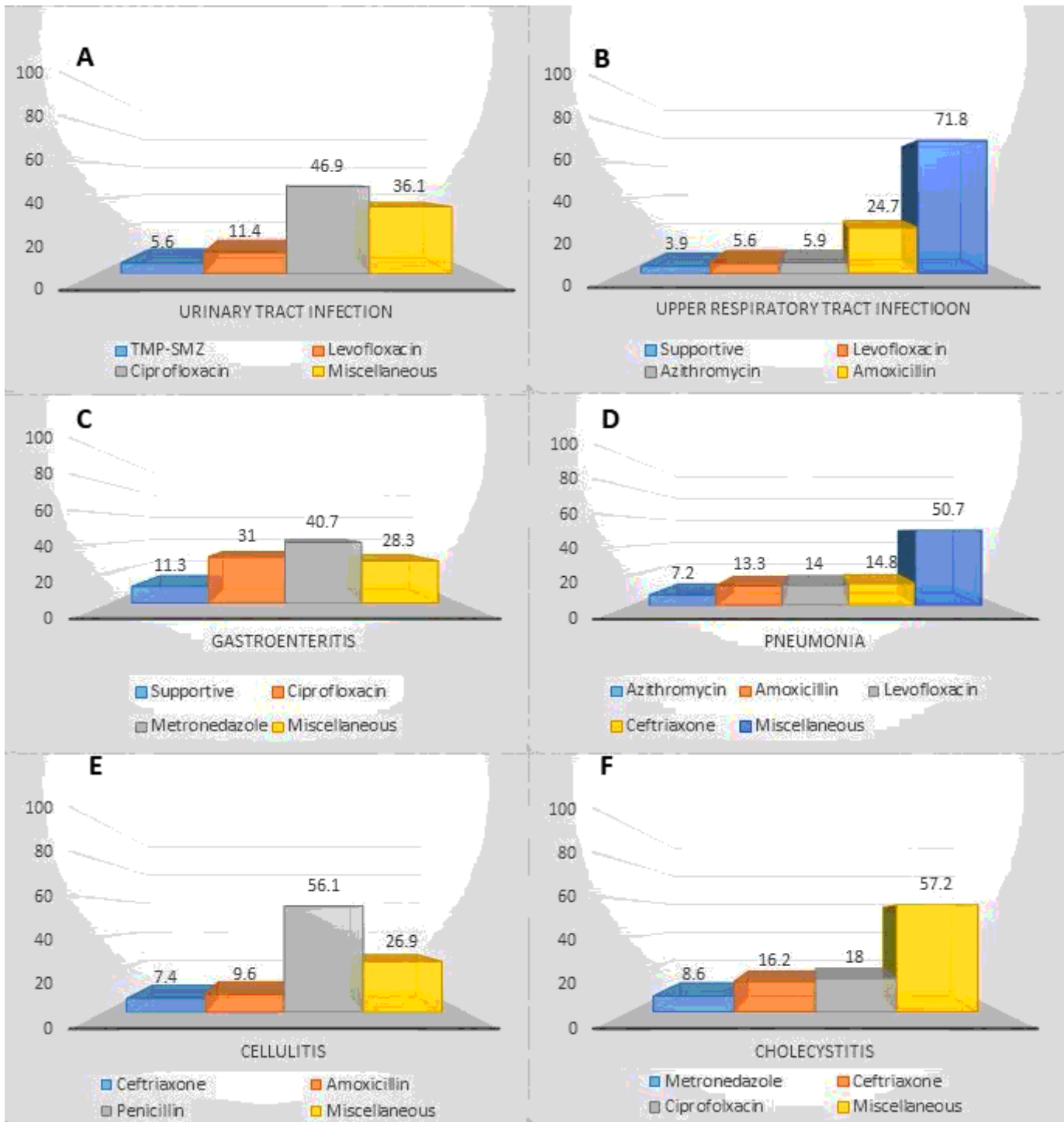


Figure 3

Empirical treatment of various infections.

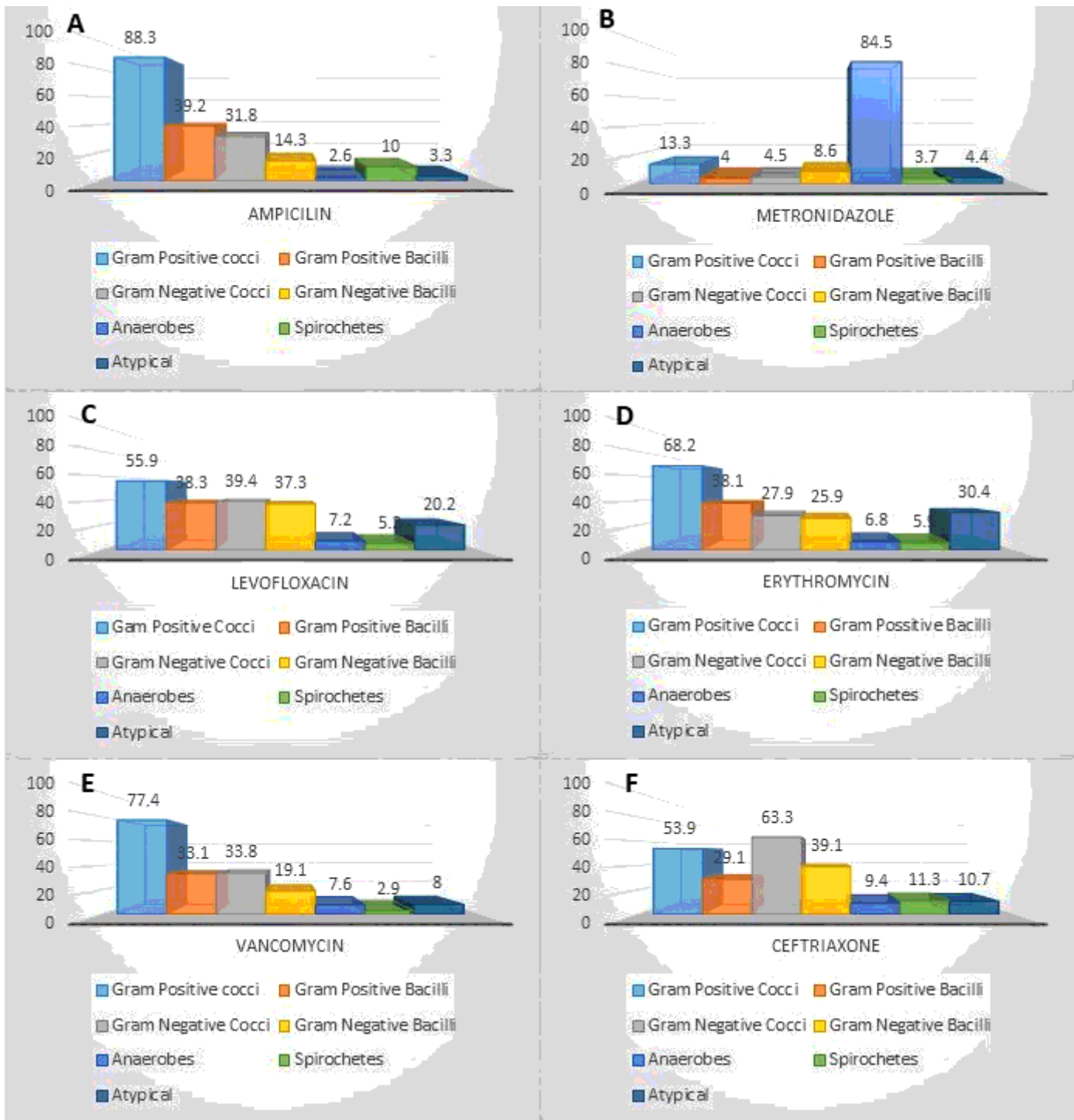


Figure 4

Antimicrobial spectrum of the drugs.