

Review

The impact of antimicrobial stewardship strategies on antibiotic appropriateness and prescribing behaviours in selected countries in the Middle East: a systematic review

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أثر استراتيجيات الإدارة المتعلقة بمضادات الميكروبات على مدى ملائمة المضادات الحيوية وسلوكيات وصفها في الشرق الأوسط: استعراض منهجي
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الخلاصة: تمثل مقاومة مضادات الميكروبات مشكلة صحية عالمية، وتمثل إدارة مضادات الميكروبات عنصراً أساسياً في سياسات المستشفيات في جميع أنحاء العالم، إلا أنه لا يوجد الكثير من المعلومات بشأن استراتيجيات التنفيذ الفعال في الشرق الأوسط. وقد أجرينا استعراضاً للدراسات التي نُفِذت في هذه المنطقة حيث طُبقت استراتيجيات مختلفة لإدارة مضادات الميكروبات من أجل تقييم مدى ملائمة مضادات الميكروبات وسلوكيات وصفها. وأجرى بحث على قواعد بيانات MEDLINE، EMBASE، والخلاصات الصيدلانية الدولية، ومحركي البحث Google Scholar، و Google. واستوفى 20 مقالاً معاً معايير الإدراج في الاستعراض؛ فُعُنت دراستان بتقييم الاستراتيجيات التي تتضمن إجراء مراجعة تطلعية مع توفير تعليقات، في حين عمدت 18 دراسة أخرى إلى تقييم الاستراتيجيات التي تتضمن مقارنة استخدام مضادات الميكروبات بالمبادئ التوجيهية. وأبرزت التوصيات المتعلقة بتنفيذ الإشراف في الشرق الأوسط أهمية إعداد وتحديث السياسات الخاصة بوصف مضادات الميكروبات على المستوى المحلي واستخدام نهج تعاونية متعددة التخصصات لتحقيق النجاح.

ABSTRACT Antimicrobial resistance is a global health problem and antimicrobial stewardship is an essential component of hospital policies worldwide yet little is known regarding effective implementation strategies in the Middle East. We conducted a review of studies carried out in this region that deployed different antimicrobial stewardship strategies to assess antimicrobial appropriateness and prescribing behaviours. A search of MEDLINE, EMBASE, International Pharmaceutical Abstracts, Google and Google Scholar was conducted. Twenty articles met the inclusion criteria; 2 studies evaluated strategies including prospective audit with feedback, while 18 others evaluated strategies including benchmarking antimicrobial utilization against guidelines. Recommendations for implementation of stewardship in the Middle East highlighted the importance of developing and updating local antimicrobial prescribing policies and using collaborative interdisciplinary approaches for success.

L'impact des stratégies de gestion des antimicrobiens sur la pertinence des antibiotiques et les comportements en matière de prescription au Moyen-Orient : analyse systématique

RÉSUMÉ La résistance aux antimicrobiens est un problème de santé mondial et la gestion des antimicrobiens constitue une composante essentielle des politiques hospitalières dans le monde. Pourtant, il existe actuellement peu d'informations sur l'efficacité des stratégies de mise en œuvre au Moyen-Orient. Nous avons passé en revue des études conduites dans la région utilisant différentes stratégies de gestion des antimicrobiens afin d'évaluer la pertinence des antimicrobiens et les comportements en matière de prescription. Une recherche dans Medline, Embase, International Pharmaceutical Abstracts, Google et Google Scholar a été effectuée. Vingt articles répondaient au critère d'inclusion, deux études évaluaient les stratégies incluant des audits prospectifs avec rétro-information, tandis que 18 autres évaluaient des stratégies incluant des analyses comparatives de l'utilisation des antimicrobiens par rapport aux procédures. Les recommandations en matière de mise en œuvre de la gestion des antimicrobiens au Moyen-Orient soulignaient l'importance de développer et de mettre à jour les politiques locales de prescription des antimicrobiens, et de recourir à des approches interdisciplinaires collaboratives, si l'on veut assurer le succès des programmes.

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Received: 03/6/16; accepted: 16/11/16

Introduction

Antimicrobial resistance is known to be one of the major threats to global health, mainly due to the prevalence of injudicious and overzealous use of antimicrobials (1). The world has reached a post-antibiotic era where major and even minor injuries can lead to multi-drug-resistant infections and result in mortality, as available antibiotic options may not be available for treatment (1). This is alarming, especially that resistant bacterial illnesses increases the cost of treatment and extends the course of therapy. As such, the duration of hospitalizations, the overall health care costs and the economic burden on families and societies worldwide will increase (1). In fact, the World Health Organization (WHO) states that multidrug-resistant bacterial infections have led to more than 8 million additional hospital stays and currently cost the health care system in excess of US\$ 20 billion (2).

Antimicrobial stewardship refers to a set of coordinated strategies that focus on promoting appropriate antibiotic use in inpatient health care settings while improving patient outcomes, ensuring patient safety, reducing pharmacy cost for antibiotics and decreasing antimicrobial resistance and the spread of infections caused by multidrug-resistant organisms (3,4). Antimicrobial stewardship programmes are typically hospital-based programmes designed to ensure that patients receive the right antibiotic, at the right dose, at the right time and for the right duration (5–7). An effective programme is one that has committed leadership and necessary human, financial and information technology resources. The literature shows that successful programmes are those that are led by a coalition between physicians and clinical pharmacists (8–10). While most research conducted is reported from centres in North America and Europe, international guidelines are currently being developed and disseminated. However, institutions in the

Middle East and the Persian Gulf region still lack firm and clear guidelines for proper antimicrobials use, which are essential for the success of local programmes due to regional variations in antibiotic utilization and prevalence of resistant organisms (10).

Antimicrobial stewardship interventions can only be successful if they meet the specific needs of the health care institution with dedicated multifaceted, multidisciplinary teams (physicians, pharmacists and nurses), administrators and policy-makers (9). These interventions include: prospective audits with intervention and feedback; implementation of formulary restriction programmes and pre-authorization requirements for specific antimicrobials within individual institutions; education; compliance with local/national guidelines and dissemination of clinical pathways; antimicrobial cycling and order forms; streamlining or therapy de-escalation; use of combination antimicrobial therapy; and dose optimization, or the switch from the intravenous route of administration to oral when indicated (7). In general, such interventions typically require essential components such as stakeholder buy-in, review of documentation systems, navigation of prescriber–pharmacist relationships and national/institutional prescribing policies (11,12).

In order to address the unique needs of individual institutions through implementation of a proactive antimicrobial stewardship programme and to provide guidance for future programme development, we conducted a review of studies that adopted different antimicrobial stewardship strategies in the Middle East region to assess antimicrobial utilization and evaluate antimicrobial prescribing behaviours within hospitals. A secondary objective was to determine core recommendations for programme development in the Middle Eastern context.

Methods

A search of MEDLINE (1948–February 2016), EMBASE (1980–February 2016), International Pharmaceutical Abstracts (1970–February 2016), Google and Google Scholar was conducted for articles assessing prescribing patterns of antibiotics and evaluating the use of antimicrobials within health care institutions in selected countries in the Middle East region. Search terms included combinations of ‘antimicrobial’, ‘antimicrobial stewardship’, ‘prescribing’, ‘utilization’, ‘resistance’, and ‘Middle East’, ‘Bahrain’, ‘Iraq’, ‘Jordan’, ‘Kuwait’, ‘Lebanon’, ‘Oman’, ‘Palestine’, ‘Qatar’, ‘Saudi Arabia’, ‘Syria’, ‘United Arab Emirates’ and ‘Yemen’. The reference lists of the articles identified were manually searched for pertinent articles that were not identified in the electronic search. Identified abstracts were included if the study was published in English and had at least 1 antibiotic prescribing pattern or its use was assessed or evaluated in a hospital inpatient setting. All populations were included. Articles were excluded if they were done in a community setting (including health centres or primary health clinics), addressed general drug prescribing patterns with no focus on antibiotics or if they did not assess use against guidelines or defined local institutional or national policies.

After title and abstract review, the full text versions of identified articles were downloaded for review. After assessment against inclusion criteria, a total of 20 articles were included in this narrative review. Data extracted from identified studies included study design, setting, interventions, comparators and results. If provided by the article, recommendations regarding programme development or implementation were also extracted.

Results

Strategies for implementation of successful antimicrobial stewardship programmes

All 20 studies collected data through patients' charts and medical file review, either retrospectively (11 studies) or prospectively (9 studies). All studies provided recommendations for successful programme development and/or implementation. Table 1 summarizes the studies in regard to the adoption by institutions of interventional strategies in order to assess and enhance antimicrobial use and prescribing behaviours by physicians (13–32).

Two studies used proactive core strategies in the form of prospective audit or point prevalence survey followed by education and feedback (13,14) to evaluate the appropriateness of antimicrobial prescribing and utilization. Amer et al. compared the prescribing appropriateness of the empiric antibiotic therapy before and after the implementation of the antimicrobial stewardship programme at their institution in Saudi Arabia (13). The primary aim of the programme was to optimize the appropriateness of antimicrobials use and thus prevent the emergence of antimicrobial resistance associated with inappropriate use. Through targeting the 5 most commonly used broad-spectrum antibiotics (piperacillin/tazobactam, imipenem/cilastatin, meropenem, vancomycin, tigecycline) in the intensive care unit setting, they prospectively compared patients who were put under the active antimicrobial stewardship programme arm with other patients who had been admitted to the same unit at that institution before the implementation of the programme in 2011 over a 6-month period during the same season. Appropriateness of empirical antibiotics was assessed by the stewardship team and evaluated according to the institution's internally developed criteria, including formulary restrictions, and following reliable

international infectious diseases clinical guidelines. Recommendations were then communicated in a verbal fashion to the intensive care unit team. The appropriateness of empirical antibiotics improved from 30.6% (15/49) in the historical control arm to 100% (24/24) in the proactive antimicrobial stewardship programme arm; the difference was statistically significant ($P < 0.05$). The rate of inappropriate antimicrobial use was reduced to 0% upon implementing the programme. There was also a significant reduction in the antibiotic utilization and direct costs in the antimicrobial stewardship programme arm. On the other hand, there was no significant clinical difference between the 2 arms of the study in terms of *Clostridium difficile* infection rate. A total of 27 interventions were made with an acceptance rate of 96.3% (13). However, this study had a number of limitations, including lack of randomization, small sample size, short follow-up duration and single institution's experience, thus affecting the generalizability of the results.

After performing a point prevalence survey over a 3-month period to assess vancomycin prescribing compliance with the Centers for Disease Control and Prevention (CDC) guidelines, Dib et al. evaluated feedback and performed an educational intervention to enhance adherence to local policies at their institution in Saudi Arabia (14). In the pre-intervention period, vancomycin utilization was deemed appropriate in only 65% (48/74) of adult patients. The investigators then implemented a continuous education and active feedback approach targeting compliance with CDC recommendations. During the post-intervention period, compliance with guidelines for vancomycin utilization increased significantly for all indicators from 65% (48/74) in the pre-intervention phase to 91% (31/34) in the post-intervention phase ($P = 0.004$). In addition, compliance with vancomycin trough level monitoring increased from 35% to 67.7% ($P = 0.0002$). The

study concluded that audit and feedback and/or educational approaches are effective in improving compliance with guidelines for antimicrobials utilization (14).

Eighteen additional studies evaluated prescribing patterns and antimicrobial utilization within hospitals in the Middle East area (15–32) by assessing compliance with local/national institutional policies or internationally endorsed clinical guidelines. Eleven (61.1%) of these reported unwarranted and inappropriate use (typically overuse) of antimicrobials. The majority of the studies concluded that prescribing habits were to blame for the discrepancies observed, and that physicians were not prescribing according to local policies and guidelines (16–26). Conversely, 6 (33.3%) studies reported adherence to guidelines and local institutional policies (27–32). These studies deemed prescribing patterns to be rational and in line with local and international standards. The reasons behind this are recorded as being the result of institutional policies, implementation of protocols or prescribing aids, or adoption of international guidelines from North America and/or Europe. Some of these studies also reported that antimicrobial stewardship initiatives (restrictive measures, antimicrobial cycling, antimicrobial switch, etc.) likely influenced adherence rates (15,24,32).

Recommendations for programme development and implementation

Specific recommendations extracted from each study are given in Table 1. All the studies we examined provided recommendations that are considered to be crucial for further enhancement of antimicrobial usage through implementation of successful antimicrobial stewardship programmes. Eight studies mentioned the importance of implementing local guidelines and policies (13,16,18,21,24,25–27). It was also suggested that these should be supported

by an infection control committee (17,23). Other studies recommended that these policies should be updated regularly and must be readily available and disseminated throughout the institution (17,20,23,24,26).

Other approaches were also mentioned. These included annual surveillance; infectious diseases team consultations (17,23,24,32) focusing on interdisciplinary collaboration; and good cross-departmental communication (22,23). In the majority of studies training of health care professionals, public health awareness and continuing medical education were considered to be important components that further enhance health care professionals' knowledge, and thus improve antibiotics use and overall prescribing appropriateness (13–15,19,21,24–26). Others highlighted the importance of the role of the clinical pharmacist in monitoring prescriptions (i.e. dosage and frequency adjustments), intervening when appropriate, and the implementation of such interventions if deemed reasonable (17,18,21,23,29,30,32). Lastly, some studies reflected upon the need for continuous use of guidelines (13,28,31) and the increased need for drug utilization reviews, audits, or strategies that include restriction policies, order forms, pharmacodynamics dose optimization and antimicrobial cycling and rotating (13–15,17,21,23,24).

Discussion

To our knowledge, this is the first review to summarize published antimicrobial stewardship interventions in the Middle Eastern context and to extract recommendations from past studies for future programme implementation. The results provide excellent background information for institutions in the region attempting to improve antimicrobial use and an insight for programme development and implementation. A total of 20 studies were identified that have

assessed at least one type of antimicrobial stewardship intervention. Two of these studies reported the use of proactive core interventions which positively affected prescribing behaviours through audit and feedback. The remaining 18 papers primarily described adherence of antimicrobial prescribing patterns to institutional, local/national, or international policies and guidelines. The end result from the studies we examined in this review was that antimicrobial utilization is a problem in the Middle East and more-proactive strategies should be developed in order to further improve the appropriateness of therapy.

The 2 papers describing proactive core strategies must be closely examined to determine how results can be applied in other settings in the region (13,14). These studies are very important, in that they demonstrate that a prospective audit and feedback approach is effective in the region, and their findings suggest that prescribers were receptive and an audit and feedback model can be established. While this approach is a core component of antimicrobial stewardship programmes in North America and Europe, there may be cultural considerations in the Middle East (physician attitudes, acceptance of collaborative practices, acceptance of pharmacist recommendations, etc.) that could limit effectiveness (8,33). These cultural differences should be further explored and any associated impact on effectiveness of programmes should be assessed. In addition, a key finding was that education seems to be central in the implementation of any programme and perhaps is important for those institutions developing programmes in areas of the Middle East where antimicrobial stewardship is considered a novel concept (34).

A number of key recommendations were extracted from the studies included in our review that provide insight into future programme development and implementation; many themes emerged from these recommendations

that warrant discussion. First, development of local policies was recommended by a large majority of the studies. The importance of this point cannot be stressed enough as antimicrobial resistance patterns vary greatly between settings and even between institutions. Therefore, antibiograms and prescribing protocols and policies are essential for continuous monitoring of outcomes at the institutional level (11,35). It is also important to note that any guideline established from other settings (i.e. North America or Europe) must be carefully reviewed for applicability before adoption in a new context.

Secondly, any policy or prescribing protocol developed must be continually updated based on current epidemiological data, including infection prevalence and antimicrobial resistance. This should be done at least annually in order to ensure guidelines and recommendations remain valid over time.

A third point that emerged from the recommendations was the importance of the collaborative approach within a multidisciplinary team. Physicians and clinical pharmacists are typically considered to be the core members of antimicrobial stewardship programme leadership (in addition to information technology personnel), however collaboration with other disciplines such as nursing, laboratory personnel, administrators and home care services will only improve stakeholder buy in and promote a culture of antimicrobial stewardship within the institution itself (9,10,36).

Considering the points discussed above, we urge institutions in the Middle East to consider the following points for programme development and implementation. First, it is important to ensure adequate baseline surveillance data is obtained, in order to guide the most appropriate type of interventions and stewardship strategies. This can be obtained through laboratory data, drug utilization trends and point prevalence surveys. In addition, it is important for

Table 1. Summary of twenty studies describing antimicrobial stewardship strategies in the Middle East

Study	Country	Design	Setting (No. of patients)	Evaluated component	Comparator	Outcome	Recommendations
Amer et al. 2013	Saudi Arabia	Comparative, historically controlled study using prospective audit with feedback	Hospital (73)	Appropriateness of prescribing the empirical antibiotic therapy	Pre/post antimicrobial stewardship programme implementation	Appropriateness improved from 30.6% to 100% (P < 0.05)	Continuous higher administration support Multidisciplinary team approach Continuous use of supplemental strategies, including education, guidelines, antimicrobial order forms, dose optimization and cycling
Dib et al. 2009	Saudi Arabia	Prospective chart audit (point prevalence survey) with educational intervention	Hospital (74)	Appropriateness of antibiotic use and effect of educational intervention on its utilization	Compliance with CDC-adapted criteria and the hospital control practices	Significant improvement in use post-intervention Compliance with guidelines improved from 21% pre-intervention to 85% post-intervention (P = 0.0001)	Emphasis on importance of active strategies, including chart audit, physician's feedback and educational efforts to decrease inappropriate antibiotic usage
Al-Tawfiq et al. 2015	Saudi Arabia	Selective and restrictive reporting of tested antimicrobial susceptibilities for key pathogens in an antimicrobial stewardship initiative, including an educational intervention before the launch of the reporting initiative	Hospital	Effect of educational intervention (change in cascade and restrictive reporting) in enhancing antimicrobial stewardship programmes and utilization of antimicrobial and clinical prescribing patterns by physicians	Compliance with local antibiograms (tracking antibiotic susceptibilities), pharmacokinetic factors and IDSA recommendations	Increased susceptibility rates to some antibiotics with reduced rates of C. difficile infection from 0.11 to 0.07 per 1000 patient days	Encouragement of use of active strategies such as restrictive reporting to further influence clinical prescribing and to permit laboratory-based contribution towards implementation of an antimicrobial stewardship programme Ongoing support from physicians is ultimately needed and they must be provided with educational interventions, including seminars, ward visits, telephone teaching and after-hours discussion
Al-Momany et al. 2009	Jordan	Prospective evaluation of patients' medical files	Hospital (236)	Degree of adherence for antimicrobial prophylaxis practice in cardiac surgery	Compliance with international guidelines	Adherence is far from optimal and inappropriate administration of antibiotics in terms of choice (1%), duration (39.4%), dose (27.9%) and dosing interval (13%)	Developing local hospital guidelines Giving the pharmacist a central role in the administration, monitoring and intervention of antimicrobial prophylaxis

Table 1. Summary of twenty studies describing antimicrobial stewardship strategies in the Middle East (continued)

Study	Country	Design	Setting (No. of patients)	Evaluated component	Comparator	Outcome	Recommendations
Al-Abri et al. 2012	Oman	Retrospective evaluation of computerized patients' case notes	Hospital (172)	Quality of care for community-acquired pneumonia management	Compliance with GCC community-acquired pneumonia guidelines	Poor adherence to guidelines in terms of prevention, diagnosis and severity assessment	Development and implementation of a locally based integrated care pathway
El Hassan et al. 2015	United Arab Emirates	Retrospective evaluation of patient records	Hospital (250)	Surgeons' adherence in terms of prescribing, selection, dosing and duration of antimicrobials	Compliance with local surgical antimicrobial prophylaxis guidelines	Poor adherence to guidelines (32.1%)	Protocol implementation Awareness and continuing medical education to target antimicrobial prophylaxis Clinical pharmacy services Cyclic auditing Deployment of clinical pharmacists in surgical wards
Aly et al. 2012	Kuwait	Retrospective evaluation of patient records	Government hospital (1112)	Physicians' adherence to antimicrobial administration	Compliance with local antibiotic policy guidelines	Poor adherence to guidelines (52.7% matching the policy and 30.4% full adherence to antibiotic administration)	Optimizing adherence by updating policies
Hammuda et al. 2013	Qatar	Point prevalence survey in the form of patient chart audit	Cancer hospital (58)	Appropriateness of use of antimicrobial agents in cancer population	Compliance with local antimicrobial prescribing policies and febrile neutropenia guidelines	Poor adherence to policies and guidelines. High prevalence of antimicrobial misuse: 57.6% of prescriptions were ordered by an approved prescriber with only 33% adherence to febrile neutropenia guidelines	Interdisciplinary collaboration and development of antimicrobial stewardship programmes
Khan et al. 2012	Qatar	Retrospective evaluation of patient medical records	Hospital (596)	Appropriateness of use of a broad-spectrum antibiotic	Compliance with local guidelines and annual surveillance periodically updated by consensus among experts	Injudicious use of antibiotics: unjustified prescriptions; inappropriate empiric prescriptions (57%); inappropriate drug modification based on the results of microbial cultures and antibiograms (22%)	Dissemination of the implemented local guidelines via staff education and widespread publication Rationalization of use in different hospital units via appropriateness in initial empiric and modification of therapy post-culture results Ongoing annual surveillance Restrictive measures such as mandatory infectious disease team consultation

Table 1. Summary of twenty studies describing antimicrobial stewardship strategies in the Middle East (continued)

Study	Country	Design	Setting (No. of patients)	Evaluated component	Comparator	Outcome	Recommendations
Hanssens et al. 2005	Qatar	Prospective observation and evaluation of patients charts	Hospital (71)	Appropriateness of use of antimicrobials and prescribing patterns of physicians	Compliance with local hospital guidelines, international guidelines and clinical judgment and experience	Inappropriate antibiotic management (52% positive cultures in 76% of patients with presumed or proven infection with only 52% change in empiric therapy post sensitivity results) Low potential for microbiological diagnostic procedures and inappropriate microbiological investigations	Urgent need for updated empiric and local hospital treatment guidelines in addition to the need for a review of antibiotic prescribing policies Monitoring of antibiotic usage Role of clinical pharmacist in assuring justified use of continuous antibiotics Implementation of empirical antibiotic treatment without any delay, based on clinical judgment, guided by local antibiograms and antibiotic resistance patterns and on de-escalating antibiotic strategy Rotating empirical antibiotic schedule to limit emergence of resistance patterns Good communication among health care professionals Implementation of infectious control practices to reduce resistance and the spread of nosocomial infections Future drug utilization reviews to assess anti-infectious management
Al-Tawfiq, 2012	Saudi Arabia	Retrospective observation of and evaluation of the pharmacy register of the annual medication utilization	Hospital	Appropriateness of use of antimicrobials	Compliance with WHO guidelines for defined daily dose of antimicrobials	Increased and unexplained usage of intravenous antibiotics; especially fluoroquinolones (from 3.5 to 82.643 defined daily dose/100 patient days) leading to emergence of fluoroquinolone-resistant bacterial strains	Specific unit antimicrobial consumption data to be able to compare with benchmarking data such as the NHSN Education and implementation of antimicrobial stewardship programme to control the use of antibiotics

Table 1. Summary of twenty studies describing antimicrobial stewardship strategies in the Middle East (continued)

Study	Country	Design	Setting (No. of patients)	Evaluated component	Comparator	Outcome	Recommendations
Al Harbi, 1998	Saudi Arabia	Retrospective evaluation of case records	Hospital (888)	Appropriateness of prescribing practices of surgeons for antimicrobial prophylaxis in the surgical ward	Compliance with the hospital local antibiotic prescribing policy	Unwarranted and overuse of prophylactic agents ($\geq 70\%$ of patients) with increased cost to the hospital	Strict enforcement of the local policy Strict surveillance and prophylactic antibiotic audit Supervision by health care team including infectious disease specialist, clinical microbiologist and clinical pharmacist for the appropriate use of antibiotics Formulary restrictions Preprinted standing orders Revision of compliance with the principles of prophylactic administration by the infection control committee
Senok et al. 2009	Bahrain	Retrospective evaluation of patients' case files	Hospital (184)	Appropriateness of antimicrobial prescribing patterns of physicians	Compliance with the AAP, CDC and the IDSA guidelines for the treatment of upper respiratory tract infections	Antibiotic overuse	Development of national guidelines based on local knowledge of clinical presentation and antimicrobial resistance patterns Integration of guidelines into structured continuing medical education courses Public health awareness campaigns actively supported by opinion leaders
Musmar et al. 2014	Palestine	Observational non-interventional prospective cohort	Government hospital (400)	Surgeons' Adherence in terms of prescribing pattern, selection, dosing and duration of antimicrobials after surgery	Compliance with the ASHP guidelines	Very low compliance in all aspects (2% compliance for studied parameters with significant p-values)	Adopting guidelines for prophylaxis; Training all health care providers
Al-Balushi et al. 2014	Oman	Retrospective cross-sectional review of prescriptions using medical files	Hospital (499)	Appropriateness of antimicrobial prescribing patterns of physicians	Compliance with CDC and WHO definition of "appropriate antibiotic prescription practices"	Similar results with studies conducted in developed countries (North America, Europe and Asia)	Encouragement of guideline-based antibiotic prescription practices Implementation of a uniform antibiotic prescribing policy based on local sensitivity patterns

Table 1. Summary of twenty studies describing antimicrobial stewardship strategies in the Middle East (continued)

Study	Country	Design	Setting (No. of patients)	Evaluated component	Comparator	Outcome	Recommendations
Zeenny et al. 2014	Lebanon	Retrospective evaluation of patient medical records	Hospital (185)	Appropriateness of use of a broad-spectrum antibiotic	Compliance with IDSA guidelines	Justified prescription for the intended use in general; antimicrobial cycling and scheduled antimicrobial switch (86% of the cases with p=0.028); Inappropriateness in dosing frequency and dosage adjustment in patients with renal failure (34.1% inappropriateness mainly due to inappropriate dose adjustment with P < 0.05)	Highlighting upon the importance of the role of a clinical pharmacist and his crucial presence in every hospital ward for dosage and frequency adjustment when necessary; Implementation of clinical pharmacists' interventions; Continuing education activities/in-services to the medical team; Mandatory supervision of antibiotic use by infectious disease specialists; Development of local antimicrobial stewardship programme
John et al. 2014	United Arab Emirates	Prospective cross-sectional review of medical records	Hospital (238)	Appropriateness of antimicrobial prescribing patterns of physicians	Compliance with WHO guidelines for upper respiratory tract infections	Rational practices in prescribing antibiotics	Encouragement of continuous use of therapeutic guidelines based on sensitivity patterns to optimize the use of antimicrobial agents
Kabbara et al. 2015a	Lebanon	Prospective observation and evaluation of electronic charts	Hospital (118)	Appropriateness of use of fluoroquinolones	Compliance with IDSA guidelines, manufacturer package inserts and clinical judgment	Appropriate prescriptions for intended use (93.2%); Inappropriateness in duration of therapy (57.6%) and dosage adjustment in renal failure patients (57.1%)	Highlighting upon the importance of the role of a clinical pharmacist in de-escalating treatment when indicated post-culture results and in sparing the use of broad-spectrum fluoroquinolones
Rehmani et al. 2014	Saudi Arabia	Quasi-experimental prospective study	Hospital (159)	Appropriateness of initial antibiotic therapy and time from recognition of severe sepsis/septic shock to first antibiotic dose delivery	Compliance with local empiric antibiotic guidelines; locally written sepsis protocol (pre/post intervention)	Improved timing and appropriateness of initial empiric antimicrobial therapy (overall reduction of 72 minutes from time severe sepsis is recognized to delivery of antibiotics); improvement by 37% in antibiotic use post-protocol implementation	Encouragement of the continuous use of local protocols and local microbiological data whilst trying to activate the protocol during the early "triage" phase

Table 1. Summary of twenty studies describing antimicrobial stewardship strategies in the Middle East (concluded)

Study	Country	Design	Setting (No. of patients)	Evaluated component	Comparator	Outcome	Recommendations
Kabbara et al. 2015b	Lebanon	Retrospective evaluation of patients' medical records	Hospital (100)	Appropriateness of use of a broad-spectrum antibiotic	Compliance with the IDSA guidelines, the Surviving Sepsis Campaign guidelines, drug information handbook dosage recommendations and clinical judgment	Appropriate prescriptions for the intended use and good adherence with national guidelines (appropriate use in 97.2% of cases empirically, and 97.2% post-culture) due to implementation of restriction policies: within 24 hours, reject or authorize use after evaluation of appropriateness) Inappropriate use related to dose adjustment in patients with renal failure	Highlighting upon the importance of the role of a clinical pharmacist in terms of: timely patient follow-up to appropriately adjust doses when necessary, and to educate other health care professionals to improve patient outcomes

AAP: American Academy of Pediatrics; ASHP: American Society for Hospital Pharmacists; CDC: Centers for Disease Prevention and Control; GCC: Gulf Cooperation Council; IDSA: Infectious Diseases Society of America; NHSN: National Healthcare Safety Network; WHO: World Health Organization.

institutions to evaluate any antimicrobial stewardship initiative on a regular basis (e.g. annually) in order to assess the impact and seek opportunities for improvement. Second, any adapted policy or guideline originating from another context must be locally validated to ensure appropriateness and applicability for the setting. While international guidelines do provide evidence-based recommendations, stewardship must be adapted to each local context and culture. Lastly, we strongly urge clinicians and researchers working in this area to disseminate their findings in the form of abstracts and publications. As demonstrated by this review, there is a great lack of data for guidance of stewardship in the Middle Eastern context, and sharing of experiences and knowledge will only work towards improving patient outcomes through appropriate use of antimicrobials.

Conclusions

Our findings show antimicrobial stewardship programmes are in their infancy in the region but that work is currently being done to further develop these programmes. Our findings also show that antimicrobial utilization is suboptimal in the region, as demonstrated by the studies we surveyed. We urge those working in Middle Eastern contexts to make antimicrobial stewardship an institutional priority and to consider recommendations identified by other centres in the region when developing and implementing new strategies. By doing so, we can work towards improving the use of antimicrobials in the region and ultimately bettering patient health outcomes.

Funding: None.

Competing interests: None declared.

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