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Review Article

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Core Elements for Successful Implementation of Antimicrobial Stewardship Programs

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ABSTRACT

Antimicrobial resistance has emerged as a serious global public health threat. One of the countermeasures to increased antibiotic-resistant bacterial infections is the use of an integrative intervention strategy for the selection and administration of appropriate antibiotics and for the monitoring of antibiotic use, collectively known as "Antimicrobial Stewardship Programs" (ASPs). However, since the medical environment and policies vary by country and medical facilities, ASPs also need to be applied to each facility and condition accordingly. The United States Centers for Disease Control and Prevention announced the core elements for hospital ASPs, which outlines the specific structural and procedural components required to implement ASPs in 2014. As multidrug-resistant bacterial infections and use of broad-spectrum antibiotics in Korea are on the rise, ASPs must be urgently applied to medical facilities for appropriate management of antibiotic use. However, there is an ongoing limitation to the immediate adoption and application of ASPs in Korean medical facilities due to the lack of medical workforce and related financial resources. To address this issue, efforts of medical professionals and government are required, and core elements that match the characteristics and circumstances of Korean medical facilities must be urgently developed.

Keywords: Antibiotics; Resistance; Superinfection; Overuse

INTRODUCTION

Antimicrobial resistance (AMR) is currently a serious problem in the medical field worldwide [1]. According to the antibiotic resistance threats report from the United States (US) Centers for Disease Control and Prevention (CDC), over 2.8 million patients are infected with antibiotic-resistant bacteria in the US annually, and over 35,000 patients die of the infection [2]. The 2014 AMR report from the United Kingdom (UK) government indicated that about 10 million people around the world will die of AMR annually if the problem is left unresolved until 2050, which is expected to be greater than the number of cancer-related deaths [3]. In 2014, the World Health Organization (WHO) declared AMR as an extremely important health crisis that threatens human life and announced that global strategies and public health actions that can help solve the AMR problem worldwide are necessary [4].

In order to overcome the increase in the number of these antibiotic-resistant bacteria, monitoring the inappropriate use of antibiotics and implementation of multiple strategies for appropriate antibiotic use are required. Integrative strategies that help in the selection of optimal antibiotics for patients requiring antibiotic treatment so that they can be administered at appropriate doses for appropriate periods of time are collectively called "Antimicrobial Stewardship Programs" (ASPs) [5]. In several aspects including reduced medical costs, improved healthcare quality, and patient safety, reduced antibiotic-resistant bacteria, and reduced incidence of pseudomembranous colitis caused by *Clostridioides difficile*, the effects of ASPs are known to bring positive results [6-11]. The Infectious Diseases Society of America published guidelines on antimicrobial stewardship in 2007 and 2016. Other countries including Australia, UK, Japan, Saudi Arabia, and Kenya established government-led guidelines that are tailored to their situations to actively implement ASPs [6, 12-17]. However, the income, medical environment, and policies vary from country to country, and even professional workforce and costs available for implementation of the ASPs vary within a country depending on type and size of medical facilities. Thus, the ASPs also need to be differentially developed and applied, taking into consideration the type and condition of each facility. In 2014, the US suggested, for the first time, specific core elements that can be used as a guide in forming structural and procedural components, which include methods of adoption and implementation of ASPs taking into consideration the financial status and workforce pool of each medical facility [18].

The number of antibiotic-resistant bacteria is currently on the rise as a serious problem in Korea due to the increase in broad-spectrum antibiotic use and amount of antibiotic use [19]. In order to address this issue, the Korean Ministry of Health and Welfare presented the "Korean national action plan on AMR (2016 - 2020)" during the 2016 National Policy Coordination Conference to propose integrative management [20], and establishment of the "second Korean national action plan on AMR (2021 - 2025) is currently in progress. Despite these efforts, Korea ranked 8th among 11 countries based on the AMR Preparedness Index presented by the Infectious Disease Society of America in 2021, and ranked 10th among 11 countries based on the National Strategy Index [16]. Due to the lack of professional workforce and financial support, the ASPs, one of the critical measures for addressing the AMR problem, are rarely applied in Korea. As each country around the world is establishing multiple policies and making efforts to adopt an ASP, Korea must urgently develop and adopt an ASP that is suitable for its situation by assessing its medical environment and the status of their national policies. Additionally, Korea needs to develop and adopt core elements that match the situation of each medical facility, similar to the US, in order to properly apply the ASPs in medical facilities. Thus, we aimed to evaluate the core elements developed in the US and the structural and procedural components of the ASPs developed in other countries, and to determine different strategies of developing the core elements suitable for the situation in Korea.

CORE ELEMENTS OF THE CDC IN THE UNITED STATES

In 2014, the US judged that proper use of antibiotics must be urgently improved, and the US CDC advised the implementation of an ASP in all acute hospitals in the US [21]. It also presented a document with seven written guidelines on core elements so that each medical facility could effectively implement ASPs and provided recommendations for implementing ASPs in all hospitals. The seven "Core elements of hospital antibiotic stewardship programs" proposed by the CDC are briefly summarized below [18].

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1. Leadership commitment

Effective leadership of the executives including the heads of medical facilities plays a very important role in the success of antimicrobial stewardship, since competency and influence of ASPs could be increased as hospital executives become aware of its importance and arrange essential resources including professionals, financial support, and information technology. For example, the heads of the facilities need to make efforts to provide the directors of ASPs with time for managing and implementing the programs every day, and to hold regular meetings for assessment of essential resources in order to achieve the objectives of the hospitals in improving antibiotic use.

2. Accountability

It is necessary to appoint a leader or co-leaders responsible for the results of ASPs activities among clinicians or pharmacists so that someone could take responsibility for managing the program and monitoring its results. Leaders need to be able to improve antibiotic use by implementing regular rounds of ASPs and by having discussions with medical professionals prescribing the antibiotics, and to report the results of stewardship activities to the executives and committee of the hospital regularly.

3. Pharmacy expertise

Participation of pharmacists is critical for leading the efforts to improve antibiotic use. Among the pharmacists, a representative who can play a leading role for the management of ASPs needs to be appointed. Particularly, pharmacists who received education on infectious diseases can offer huge assistance in implementing ASPs in larger hospitals and healthcare systems.

4. Action

As one of the measures to improve antibiotic use, the implementation of intervention activities is required including limitations in the prescription of antibiotics, use of pre-approval system, conduct of prospective surveillance, and provision of feedback. For example, broad interventions include considering the importance of antibiotics during prescription, selection of appropriate antibiotics, surveillance of period of use, and re-evaluation of the importance and adequacy of continuous use of antibiotics after 48 hours of use. In addition, staff-pharmacy interventions include the automatic transition of intravenous antibiotics to oral antibiotics at the appropriate time, drug level monitoring, automatic warning for unnecessary repetition of antibiotic prescription, notification for antibiotic use for more than a reasonable period, and detection of interactions between antibiotic-related drugs and other drugs. Finally, infection- and syndrome-specific interventions could be focused on diagnostic assessment, use of appropriate empiric antibiotics, and re-evaluation of prescribed antibiotics. Microbial testing and antimicrobial susceptibility test are important for the selection of the appropriate empiric antibiotics based on the sites of infection such as community-acquired pneumonia, urinary tract infection, and skin and soft tissue infection. Mediation of cases that do not require antibiotic use including asymptomatic bacteriuria and identification of contaminants is critical to reduce unnecessary antibiotic use.

5. Tracking

In order to track the application of ASPs, monitoring of the antibiotics used in hospitals and patterns of antibiotic-resistant bacteria and performance of objective evaluation and analysis are required. It is also important to collect and analyze the data on the antibiotics used in each medical facility at the government level. For example, the US CDC collected and reported the data of monthly antibiotic use electronically to the National Healthcare Safety Network, the

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integrative internet management system of patient safety and healthcare worker safety, in order to develop a system that could analyze the usage of specific antibiotics by region [22].

6. Reporting

The results of ASPs need to be provided to the prescribing physicians, pharmacists, nurses, and medical facility executives, with regular updates on the information about antibiotic prescription, antibiotic-resistant bacteria, and treatment of infectious diseases by reflecting all national and regional issues [23]. Information about the incidence of antibiotic-resistant bacterial infections is prepared by collaborating with the hospital's microbiology lab and infection control and healthcare epidemiology department. Then, these data need to be summarized with information on the frequency of antibiotic use and then submitted to the medical facility executives and related medical professionals.

7. Education

Education about antibiotic prescription and antibiotic-resistant bacteria is a core element of comprehensive efforts for improving antibiotic use in hospitals. The different methods of education delivery include lectures, posters, flyers, newsletters, and electronic communication with related departments about antibiotic use, which are most effective when combined with the application of ASP interventions and measurement of outcomes [6]. Education using the handshake stewardship approach could be effective, where an antimicrobial stewardship team composed of pharmacists and doctors review the prescribed antibiotics and immediately provide direct and personalized feedbacks during their rounds. In addition, the education was most effective when information on the related activities of the department were delivered after customization, such as providing guidelines on antibiotic prescription for community-acquired pneumonia to prescribing physicians and offering education about culturing techniques to nurses. Patient education can also play an important role in ASPs, where patients need to know which antibiotics they are using, the reason for using these antibiotics, and the treatment-related signs and symptoms that they need to share with the provider. As part of the patient education efforts, the roles of nurses are important, in that they need to participate in developing patient education materials for appropriate antibiotic use.

Meanwhile, only a few countries outside of the US specifically present guidelines on these core elements. According to a consensus report written in 2018 through a review of 48 references for clarifying the definitions of core elements as attention to ASPs worldwide increased, the seven core elements that could be related to the implementation of ASPs in hospitals around the world are as follows: senior hospital management leadership toward antimicrobial stewardship, accountability and responsibilities, expertise in the field of infection management, education and practical training, other actions aiming at responsible use of antimicrobials, monitoring and surveillance (on a continuous basis), and reporting and feedback (on a continuous basis). These were very similar to the seven "Core elements of the hospital antibiotic stewardship programs" of the US CDC, although the checklists made for evaluation of each core element included more comprehensive contents than those provided by the CDC [24, 25].

Based on the guidelines on the "Core elements of hospital antibiotic stewardship programs," the US CDC is currently publishing additional guidelines for nursing homes, outpatient settings, and small hospitals with poor workforce and infrastructure, aside from those for large hospitals [26-29]. The up-to-date CDC guidelines on the core elements of Antibiotic Stewardship for Outpatient Setting and Resource-Limited Settings are briefly outlined in **Table 1**.

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Table 1. Core elements of antibiotic stewardship in outpatient setting and resource-limited settings by US CDC

Core elements of outpatient antibiotic stewardship programs [26]
1. Commitment
Demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety.
2. Action for policy and practice
Implement at least one policy or practice to improve antibiotic prescribing, assess whether the policy is effective, and modify it as needed.
3. Tracking and reporting
Monitor the antibiotic prescribing practices and provide regular feedback to clinicians, or have clinicians assess their own antibiotic prescribing practices themselves.
4. Education and expertise
Provide educational resources to clinicians and patients on antibiotic prescribing, and ensure access to needed expertise on optimizing antibiotic prescribing.
Core elements of antibiotic stewardship programs in resource-limited settings [27]
1. Foundational structures of ASPs in acute care facility
Single focal point with responsibility for the program.
Support from hospital leadership.
2. Beyond the foundation: a stepwise approach to building a stewardship program
Form an antibiotic stewardship committee.
Start with a single priority area of the ASPs.
Ensure appropriate policies or guidelines are in place, especially for the priority area.
Educate staff and publicize stewardship campaign.
Implement stewardship activities targeted at the priority.
3. Monitoring and evaluation of ASPs
Monitoring and evaluating processes and impact.

US, United States; CDC, Centers for Disease Control and Prevention; ASPs, Antimicrobial Stewardship Programs.

Currently, the US is conducting annual reviews on the level of stewardship implementation in medical facilities participating in the survey by creating a checklist for each hospital to self-check the application of the seven core elements of antimicrobial stewardship [30]. Efforts are being made at the national level to manage the expansion and application of high-quality stewardship program including presentation of successful cases of ASPs at the state and hospital levels through the CDC website as well as to provide financial support necessary for the implementation of the core elements to local hospitals in order to train pharmacists and doctors. As a result, the percentage of hospitals in the US that meet the standards of the seven core elements increased from 40% in 2014 to 89% in 2019 [31]. The broad-spectrum and unnecessary antibiotic use and *Clostridioides difficile* infection rate decreased after the application of ASPs in medical facilities [11, 32-34].

The application of ASPs is essential in all hospitals prescribing antibiotics, from primary hospitals to tertiary general hospitals. However, as in the US, the workforce and financial resources in Korea available for implementation of ASPs vary based on the types of medical facility. Thus, it is necessary to appropriately develop core elements that could be implemented for each type or condition of medical facility and create a suitable checklist for the application of ASPs to resource-limited settings.

TOOLKITS FOR ASPS IN THE UNITED KINGDOM

Guidelines were also developed for the application of ASPs to medical facilities in the UK. The UK presented the structural and procedural components for ASP application and the necessary resources, such as the toolkit. The Antimicrobial Self-Assessment Toolkit was the first toolkit developed by the National Pharmacy Reference Group of the UK in 2010 for assessing antimicrobial resistance and healthcare associated infection [35]. This is a guideline developed for the first time to self-evaluate the application of ASPs to acute hospitals in the UK. It presented the structural and procedural components that need to be

prepared for introduction of ASPs to medical facilities in seven domains, which contained contents similar to the core elements of the US excluding contents about leadership commitment and accountability. The second toolkit developed in the UK was the Start Smart, Then Focus Antimicrobial Stewardship Toolkit for English Hospitals in 2011, which was used for the application of an ASP in secondary medical environment. In March 2015, its revised version was released [36, 37]. Among the toolkits developed in the UK, this toolkit has the most similar meanings to the core elements of the US. The structural and procedural components for the application of ASPs in UK medical facilities were presented first into six categories. Next, the procedural components for appropriate selection and prescription of antibiotics were divided into "Start Smart" and "Then Focus" categories in order to present more specified guidelines. The final toolkit developed in the UK was Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) Toolkit, which is an online education material made in 2012 to promote the application of ASPs in primary medical facilities in the UK that lack professional workforce. It was developed by the Public Health England together with the Royal College of General Practitioners (RCGP) and other professional societies and operated by the RCGP website [38-40]. The TARGET Toolkit is an online training resource for the application of ASPs, which is a separate concept from the structural and procedural components for application of ASPs mentioned earlier. TARGET Toolkit contains various leaflets that include lecture videos that could be used by physicians when prescribing the antibiotics, self-checklist for implementation of ASPs, guidelines on antibiotic prescription based on the types of infection, and educational materials that could affect social norm and attitudes of patients toward antibiotic prescription. The toolkits are regularly updated to assist general practitioners of primary medical facilities in implementing ASPs [41]. The toolkits developed to date in the UK for the application of the ASP are briefly outlined in **Table 2**.

In order to promote the application of ASP in medical facilities, the UK established an index related to the antibiotic use aimed at examining the appropriateness within 72 hours of antibiotic prescription, promoting the application of ASP, and reducing indiscreet antibiotic use. This index was established as part of the national health service commissioning for quality and innovation that provides up to 2.5% incentives depending on the assessment results [42].

Since the rate of antibiotic prescription in Korea is extremely high in primary medical facilities at the clinic level [43], it will be helpful to develop online resources for the application of ASPs such as the UK TARGET Antibiotics Toolkit to ensure appropriate antibiotic use and to assist physicians in primary medical facilities in actively utilizing these resources. It is also important to develop a plan such as the UK incentive program that involves the conduct of regular inspections and monitoring of ASP application in each medical facility and to provide incentives based on the assessment results, which would together promote the application of ASPs.

ESSENTIAL ELEMENTS AND STRATEGIES REQUIRED FOR ASPS IN AUSTRALIA

In Australia, where about 70% of total medical services are offered in government-funded public hospitals, the Australian commission on safety and quality in health care presented guidelines on the successful adoption of ASPs in 2011 [15]. These guidelines were presented in the following categories: structure and governance, essential strategies for all hospitals, and ASP activities according to local priorities and resources. In 2018, they were updated and

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Table 2. Toolkits for antimicrobial stewardship programs in the United Kingdom

Antimicrobial self-assessment toolkit for acute hospitals [35]
1. Antimicrobial management within the trust—structures and lines of responsibility and accountability—and high-level notification to the board
2. Operational delivery of an antimicrobial strategy—operational standards of good antimicrobial stewardship
3. Risk assessment for antimicrobial chemotherapy
4. Clinical governance assurance
5. Education and training—training needs and delivery of education and training for all medical professionals who issue, prescribe, and administer antimicrobials
6. Antimicrobial pharmacist—systems in place for ensuring their optimum use
7. Patients, carers, and the public—information needs of patients, carers, and the public
Start smart-then focus antimicrobial stewardship toolkit for English hospitals [36]
1. An assessment of the Trust's antimicrobial stewardship activities
2. An antimicrobial stewardship management team/committee
3. A ward-focused antimicrobial team
4. Evidence-based antimicrobial prescribing guidelines
5. Quality assurance measures/audits and feedback
6. Education and training
Start smart
1. Start antibiotic upon detection of bacterial infection.
2. Use local guidelines.
3. Document on the drug chart and medical notes the clinical indication, duration or review date, route, and dose.
4. Obtain cultures prior to prescribing antibiotics.
5. Single-dose surgical prophylaxis must be provided where evidence supports.
Then focus
1. Review clinical diagnosis and the continuing need for antibiotics within 48 hours and make the "Antimicrobial prescribing decision."
2. The five decision options are to stop/switch from intravenous to oral antibiotics or /change/continue/move to the outpatient parenteral antibiotic therapy
TARGET antibiotic toolkit [40]
1. Interactive workshop presentation or e-Module for personal learning
2. Leaflets to share with patients
3. Audit toolkits
4. National antibiotic management guidance
5. Training resources
6. Resources for clinical and waiting areas
7. Self-assessment checklist

Table 3. Essential elements and strategies for ASPs in Australia

Essential elements and strategies for ASPs [44]
Structure and governance
1. Ensuring that antimicrobial stewardship resides within the organization's quality improvement and patient safety governance structure
2. Establishing a multidisciplinary antimicrobial stewardship team that includes, at least, a lead doctor and pharmacist
3. Providing the necessary human, financial, and information technology resources for implementing the antimicrobial stewardship activities
4. Ensuring ongoing education and training for prescribers, pharmacists, nurses, midwives and consumers about antimicrobial stewardship, antimicrobial resistance, and optimal antimicrobial use
Essential strategies
1. Implementing clinical guidelines consistent with the Therapeutic Guidelines: Antibiotic that take into account the local microbiology and antimicrobial susceptibility patterns
2. Implementing formulary restriction and approval systems that include restriction of broad-spectrum and later-generation antimicrobial administration in patients in whom their use is clinically justified
3. Reviewing the rate of antimicrobial prescriptions with provision of interventions and direct feedback to the prescriber
4. Implementing point-of-care interventions (including directed therapy, intravenous-to-oral switching and dose optimization)
5. Ensuring the provision of clinical microbiology service
6. Monitoring antimicrobial use and outcomes, and reporting to clinicians and management

ASPS, antimicrobial stewardship programs.

presented as structure and governance and essential strategies for essential elements and strategies for ASPs [44]. These categories were similar to the core elements of the US and were divided into structural aspect and procedural aspect, which are briefly outlined in **Table 3** [44].

Similar to the core elements in the US, the structure and governance for ASP application in Australia also indicates that leadership of the directors and clinicians of medical facilities,

in terms of management of healthcare-associated infections and management for antibiotic prescription and reduced antimicrobial resistance, could improve patient safety and quality [44]. The application of ASPs requires formation of a multidisciplinary antimicrobial stewardship team with a doctor or a pharmacist as a director as well as sufficient supply of workforce, financial, and information technology resources for the development of technologies such as an online antibiotic prescription approval system and antibiotic use surveillance system. In addition, regular education needs to be provided to prescribing physicians, pharmacists, nurses, and patients receiving the prescription, which are similar to the contents of the leadership commitment, accountability, and education categories of the core elements of the US. With regard to the strategies for ASP application, the main contents include proper selection of antibiotics following the guidelines, prescription of antibiotics based on the guidelines on prescription approval and restriction, and review of used antibiotics after the prescription via monitoring and reports, which are similar to the contents of the action, tracking, and reporting categories of the core elements.

Australia also differentially presents the structure and governance for ASP application based on the type of medical facility, taking into consideration the medical facilities' lack of professional workforce and financial support [44]. For example, the role of an ASP director in a medical facility needs to be fulfilled by an infectious disease physician, pharmacist, or clinical microbiologist. However, if there is lack of professional workforce, a local or network/district pharmacist or facility manager fulfills the role and receives advice from the local or network/district infectious disease physician or clinical microbiologist. In another case, the facility manager is supposed to direct ASPs with help from visiting clinicians or pharmacists. In addition, the composition and role of the antimicrobial stewardship team and the responsibility of leadership commitment are presented differently depending on the type of medical facilities.

To promote the application of antimicrobial stewardship to each medical facility, Australia has included assessment of antimicrobial stewardship application based on the national safety and quality health service standards guidelines developed by the Australian Commission on Safety and Quality in Healthcare (ACSQHC) in 2013, along with the quadrennial implementation of mandatory hospital accreditation [45]. In addition, the antimicrobial use and resistance in Australia surveillance system established by the ACSQHC has been used to monitor AMR incidence in medical facilities as well as the patterns and trends of antibiotic use since 2014. Since 2016, national data on critical antimicrobial resistances have been provided [46].

CURRENT STATUS AND FUTURE PERSPECTIVES OF THE CORE ELEMENTS OF ASPS IN KOREA

To overcome the AMR problem at the national level, Korea announced “National action plan on AMR 2016 - 2020 (Korean)” in 2016. It prepared detailed plans that helped reduce the rate of antibiotic use by 20% until 2020 compared to 2015, which focused on the following six main areas: appropriate antibiotic use, prevention of the spread of antibiotic-resistant bacteria, reinforcement of the surveillance system, improvement of awareness, expansion of infrastructure and research and development, and activation of international cooperation [20]. The conference hosted by the Korean Society for Antimicrobial Therapy in April 2021 announced the evaluation of the implementation of the “National action plan on AMR 2016

- 2020 (Korean)" by "AMR forum on national action on AMR and development of successful strategies," which is the service task of the Korea Disease Control and Prevention Agency (KDCA) jointly implemented since 2020 by the Korean Society for Antimicrobial Therapy, Korean Society of Infectious Diseases, and Korean Society for Healthcare-Associated Infection Control and Prevention. In addition, it announced the detailed strategies and action plans during the second national action plan on AMR 2021 - 2025. The achievements of the "National action plan on AMR 2016 - 2020 (Korean)" include the establishment and operation of AMR surveillance system that meets the WHO-recommended international standards and development of guidelines on proper antibiotic use. However, there are still unsolved problems including the absence of a medical service fee system of ASPs, lack of professional workforce, and absence of guidelines that are tailored to the situation in Korea. In addition, the conference mentioned that professional training and systemic support need to be provided through the second Korean national action plan on AMR for adoption of ASPs in the Korean medical facilities.

Effective intervention strategies of ASPs include prospective monitoring of antibiotic use, provision of feedback, and use of a pre-approval system [47]. Above all, the roles of teams and directors operating the ASPs are important in the establishment of a management system for the implementation of these strategies. The ASPs operated by infectious disease physicians in a Korean university hospital in 2018 significantly reduced the antibiotic use in hospitals and the incidence of antibiotic-resistant bacterial infections [48]. The important strategies used in the operation of ASP developed by multiple countries mentioned above also included the importance of training and education of professionals related to antibiotic prescription including infectious disease physicians and infection drug pharmacy specialists. However, only a few infectious disease physicians and trained clinical pharmacists could play a significant a role as the director of ASPs in Korea. As of November 2020, only 350 infectious disease physicians are registered in the department of internal medicine or department of pediatrics, and only 86 infection drug pharmacy specialists are available. In the US, only 1.76 out of 100,000 people were infectious disease physicians as of 2017, and it increased by 42% from 6,424 in 2008 to 9,136 in 2018. Therefore, there is still lack of infectious disease physicians due to the emerging infectious diseases and antibiotic-resistant bacterial infections, and more professionals will be needed in the future [49, 50]. However, the number of infectious disease physicians in Korea as of 2019 is 0.47 out of 100,000 people, which is fewer than half of those in the US. Out of 100,000 people, fewer than 0.01 infectious disease physicians are assigned in Gyeongsangbuk-do and Ulsan metropolitan city [51].
In 2018, a survey was conducted on the status of ASPs in Korean hospitals with a 500 beds capacity or greater, and as a result, the median number of medical personnel participating in ASPs was 3 (interquartile range [IQR], 1 - 5), and only 6.0% (5/84) of hospitals had full-time workers for ASPs [52]. In most hospitals, intervention for ASPs was limited to antimicrobial restriction for designated antibiotics due to lack of time, personnel, and appropriate compensation [52]. Subsequently, in 2020, a survey was conducted on the status of ASPs in Korean hospitals with a 150 beds capacity or greater. As a result, in secondary and primary care hospitals there was no predominant medical personnel for ASP, and in tertiary care hospitals, the median number of medical personnel for ASPs was 0.32 (IQR, 0.09 - 0.72) full-time equivalent (FTE) per 1000 beds [53]. According to the report that calculated the estimated human resources required for an ASP in Korean hospitals in 2020, the personnel requirement was calculated as 1.20 (IQR, 1.02 - 1.38) FTEs per 100 beds and 2.28 (IQR, 1.93 - 2,62) FTEs per 100 patients who underwent antibiotic therapy, respectively [54]. Compare to these results, there is a shortage of manpower for ASPs at medical facilities in Korea. In

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order to address this issue, it is necessary to review the medical fees for infectious disease specialists in the medical facilities as well as to develop a reasonable system and provide an economic compensation in order to encourage more doctors to select infectious diseases as their field of expertise. Moreover, the infection drug pharmacy specialist workforce must be expanded and a good compensation system for antibiotic management must be developed. In 1997, the Duke University School of Medicine in the US established the Duke Infection Control Outreach Network (DICON) in order to form networks in medical facilities in regions that lack professionals assigned to handle infectious disease management tasks, provide educational materials related to the proper prescription of antibiotics and infection management, and provide education and training to infectious disease specialists who can regularly visit local medical facilities and implement infection management programs. Based on this, the Duke Antimicrobial Stewardship Outreach Network (DASON) was established in 2013; in 2018, the Duke Center for Antimicrobial Stewardship and Infection Prevention was established as an integration of DICON and DASON to provide education, consultation, and Duke hospital services, and to conduct research activities. Such professional workforce sharing system using networks could help in infection management and ASP implementation in medical facilities lacking professional workforce [55]. Korea would also need to prepare multiple plans to address the lack of professionals such as a networking system that allows sharing of medical professionals from general hospitals to small and critical-access hospitals, part-time contracts with professionals, and operation of ASPs through remote medical services.

In order to apply the ASPs to medical facilities in Korea, the lack of financial resources needs to be resolved as well. In March 2018, the Ministry of Health and Welfare investigated the hospital-level or higher-level of medical facilities in Korea in terms of healthcare-associated infection control including infection control system, infrastructure including workforce and facilities, and infection control activities. Results showed that only 53.2% of nursing homes isolate patients with multidrug-resistant bacterial infection, and only 39.4% of nursing homes conducted identification of risk factors for infection. Moreover, only 1.6% of nursing homes with intensive care units and operating rooms participated in the national healthcare-associated infection surveillance system [56]. “National Action Plan on AMR 2016 - 2020 (Korean)” mentioned the expansion of hospitals for installation of infection control rooms and the application for medical facility accreditation for expansion of infectious disease specialists and preparation of fee compensation system for ASP management activities. However, the cost of ASPs have not yet been established for 5 years, including multidisciplinary treatment fees for the intensive management of restricted antibiotics, multidisciplinary treatment fees for managing high-risk patients, and the antibiotic management cost. Accordingly, in order to implement ASPs within a medical facility, it is necessary to provide financial and human resources for ASPs on its own, but this is difficult in reality. Currently, the categories related to antimicrobial stewardship are included in the standards of 3rd cycle of acute care hospital accreditation program. However, the infection prevention and control system at the hospital level includes only the operation of antibiotic use management committee as a subcategory. On the contrary, information on the team members, directors, and tasks of ASPs are not organized in detailed categories. Due to problems related to the professional workforce and financial resources necessary for implementing ASPs, most medical facilities are not prepared to form an appropriate professional workforce for antibiotic use management. Moreover, even if there are other available medical professionals, they mostly take charge of other clinical works and subordinately take responsibility in antibiotic management, making it difficult to operate ASPs in a real-world setting. Some solutions to this issue include regular assessment of

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ASPs in each medical facility, provision of adequate incentives such as in the UK, inclusion of contents related to ASP implementation in the hospital accreditation standards, and rendering ASP application mandatory in hospitals like the US and Australia [42, 45, 57]. In the long term, financial support for adoption of ASPs will bring more economic benefits through reduction of medical costs related to antibiotic use in the future [58-61].

Finally, the structural and procedural components of ASPs suitable for the situations in Korean medical facilities need to be developed in order to successfully implement this program in Korea. Currently, the "Guideline of implementing antimicrobial stewardship program in Korea" has been developed in 2021 as a part of academic research and development service tasks by the KDCA [62]. Based on this, Korea also needs to develop detailed core elements and checklists for the application of ASPs in medical facilities such as in the US, UK, and Australia. Data provided by the Korean national statistics portal website (Korean Statistical Information Service) on the status of medical care institutions by type mention that as of February 2021, there are 45 tertiary hospitals, 319 general hospitals, 1,409 hospitals, 1,466 nursing homes, and 33,531 clinics under operation. In the 2019 results of the evaluation of drug reimbursement adequacy provided by the Health Insurance Review and Assessment Service, the prescription rates of antibiotics in all visiting patients by type of medical facility (ratio of antibiotic prescription case compared with days of hospital visit) were as follows: 22.37% in clinics, 18% in hospitals, 8.64% in general hospitals, and 3.66% in tertiary hospitals [43]. Therefore, development of core elements and distribution of toolkits must be urgently carried out for the adoption and operation of ASPs in Korean medical facilities with insufficient professionals and resources, where antibiotic prescription rate is high especially in clinics and hospitals. For the promotion of ASP application in medical facilities, mandatory education about ASPs on a regular basis and provision of necessary resources to medical facilities through assessment and feedback about the operation of ASPs are necessary.

CONCLUSION

Currently, several countries are preparing AMR management solutions at the national level to deal with increasing number of antibiotic-resistant bacterial infections due to overuse of antibiotics. Adoption and operation of ASPs in medical facilities are essential for the management of appropriate antibiotic use. In Korea, the biggest obstacles in the implementation of ASPs are the lack of professional workforce and financial support. To address these challenges, government departments should strive to establish policies for the allocation of medical fees for antibiotic management, education for training professionals, compensation for professionals, and introduction of governmental-led accreditation system or incentive system for activation of ASPs. In addition, academic circles should take the lead in developing core elements and toolkits suitable for the characteristics and situations of Korean medical facilities, and cooperate with government departments to develop curriculums for training professionals and implementing of ASPs in medical facilities.

SUPPLEMENTARY MATERIAL

Korean version.

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