

Research Article

The Influence of Antibiotic Stewardship Program on Indoor Patients in Asia. A Systematic Review

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Abstract:

Background: Antibiotic resistance is a growing global threat driven by antibiotic overuse. Antibiotic stewardship programs (ASPs) are a key strategy to optimize antibiotic prescribing and combat resistance.

Objective: To systematically review the impact of ASPs on clinical and economic outcomes among hospitalized patients in Asia.

Methods: We searched PubMed, Google Scholar, and PakMediNet for studies published in 2017-2021 that quantified ASP outcomes. Studies on costs, antibiotic use, length of stay, and mortality were included.

Results: 18 studies met inclusion criteria. 13 (72%) reported decreased costs after ASP implementation, with net savings of up to \$12,829 USD per patient. All studies showed reduced antibiotic use, especially carbapenems. 8 (44%) found shorter lengths of stay and 10 (56%) reported lower mortality rates with ASPs.

Conclusions: ASPs improve clinical outcomes and reduce costs and antibiotic resistance in Asian hospitals. More research is needed on ASP knowledge and implementation in outpatient, primary, and secondary care settings.

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INTRODUCTION:

Antibiotic resistance is a worldwide threat. Multi-drug resistant bacteria are gaining importance, as they are becoming the source of infections in all patients of all age groups and causing deaths. According to CDC, 23000 deaths occur in the USA per year due to infections caused by MDR⁽¹⁾. Antibiotic

stewardship program is the best way to supervise the usage of already present antibiotics, other ways to kill bacteria, and to develop alternatives. WHO has explained the requirement to involve professionals, civil society, and multiple organizations, to consider the local factors that drive substandard use in different

healthcare settings⁽²⁾. Guidelines and recommendations for the proper implementation of ASPs have already been published. The objective is to make a systematic review to update, evaluate, and broadly summarize the clinical and economic impact of ASPs including the work on pediatric patients in Asia.

ASP aims to improve patient clinical outcomes, to decrease antimicrobial resistance and healthcare cost by promoting fair use of antibiotics. Some core elements of ASP include leadership commitment, physicians check, medical expertise, and education of doctors and patients. ASP may require extra sources, like hospital personnel as well as equipment so that it can be effective. The costs related to these extra sources can be a potential hindrance where ASP is not implemented yet.

MATERIALS AND METHODS:

The Prisma checklist was used as a protocol to conduct this systematic review. The inclusion criteria were articles from the last 5 years (2017-2021), articles with quantitative statistics, grey literature and published articles, and full-length articles only. The exclusion criteria were articles on outdoor/ community infections, non-English articles, articles on antifungals / antivirals, animal/ agriculture articles, and studies from non-Asian countries.

The information sources searched were Google Scholar, PubMed, and PakMediNet on 15-6-2021. Boolean operators were used in the search strategy with keywords including "antibiotic stewardship program", "Asia", "antimicrobial consumption", and "cost". Additional searches used the terms "ASP AND mortality rate" and "ASP AND length of hospital

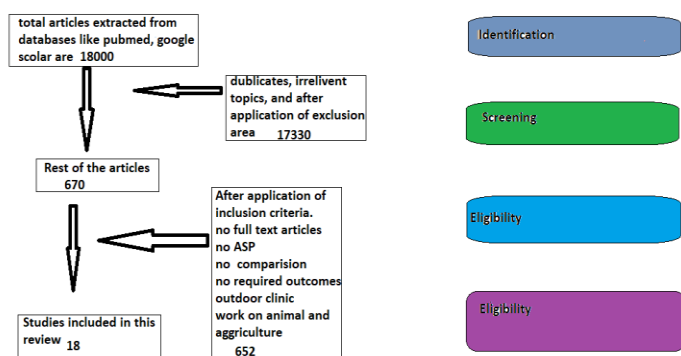
stay". After searching the databases, 18,000 articles appeared initially. Applying filters and exclusions left 670 articles, and after applying inclusion criteria and other factors, 18 total studies were selected for review.

Data collected from each study included the year, country, study design, and outcomes in the form of pre and post-ASP implementation. The outcomes gathered were cost, length of hospital stay, antibiotic consumption, duration of therapy, and mortality rate. Statistical significance such as p-values and confidence intervals were noted when provided.

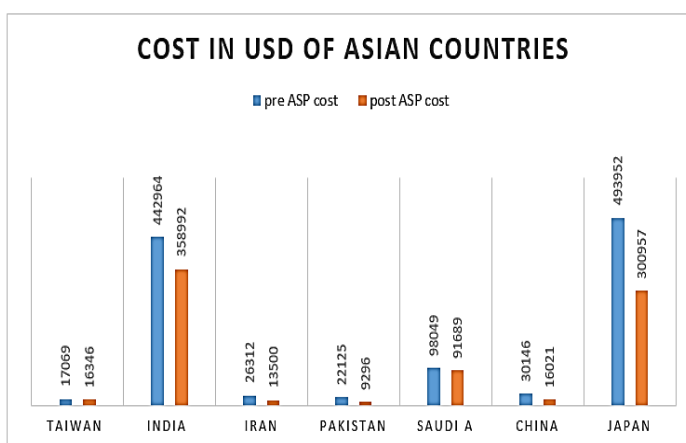
RESULTS:

This review is done by taking the articles of the last 5 years. A total of 18000 articles were extracted from different databases which are google scholar, PubMed, and PakMedinet. After removing duplicate, irrelevant articles, and applying inclusion and exclusion criteria, articles which are taken for review are 18. Cost is estimated by almost 13 out of 18 (72%) articles (1,2,3,4,5,7,8,10,11,12,13,14,18). All the articles studied (100%) give statistics about antimicrobial consumption mostly in the form of daily defined doses per 1000 patients. Antibiotic consumption differs according to the antibiotics like consumption of colistin decreases post-implementation of ASP while linezolid consumption increases. Length of stay is explained in almost 8 out of 18 (44%) studies (3,4,6,11,12,14,15,16). The mortality rate is studied in 10 out of 18 studies which is 58% (1,3,4,5,10,12,13,14,15,16). 2 out of 18 studies give information about the Clostridium difficile infection. (4,18). 12 out of 18 studies give information on more than two

variables. 2 studies compare the outcomes in pediatrics, showing a decreasing trend in cost, length of stay, and infection rate. We did this review to get the quantitative results of a total of 18 studies which are from Asian countries, between 2017- 2021.

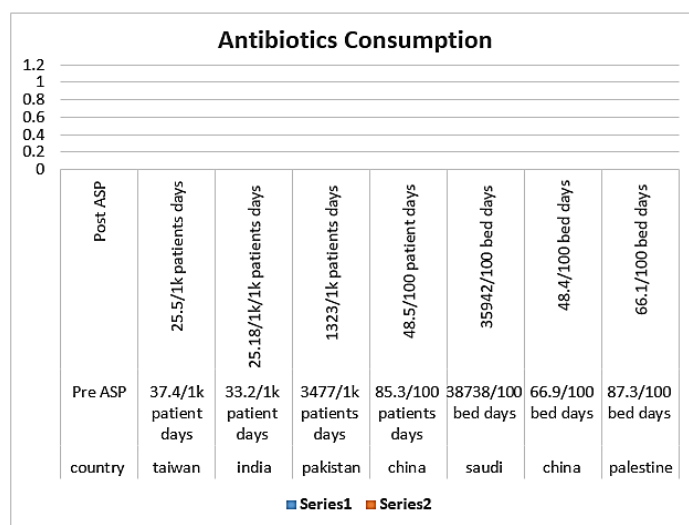


13 studies explained the difference in cost before and after the implementation of the antibiotic stewardship program in indoor patients between 2017-2021. Almost all the studies give the information, showing the prominent decrease in cost after the application of the antibiotic stewardship program. A study done in Pakistan in 2018 showed cost in US\$ before ASP was 22125US\$ decreased to 9296US\$, and there is a net saving of 12829US\$ after the implementation of ASP (5). This cost reduction is due to the decreased usage of antibiotics, early de-escalation of antibiotics, and switch from IV to oral regimen.

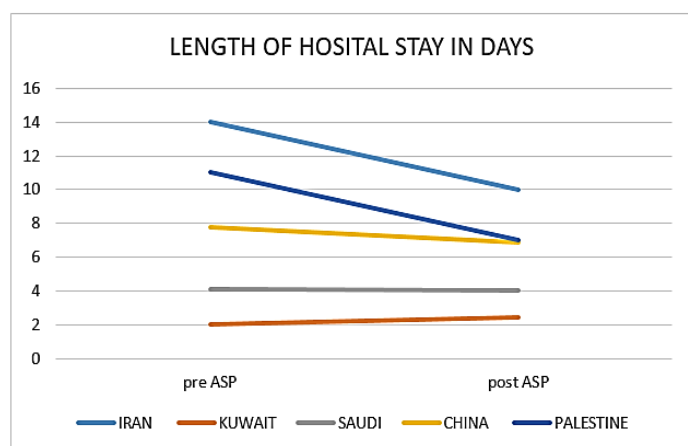


Consumption of the antibiotic is explained in all 18 studies. Consumption of different antibiotics is studied in different studies. One antibiotic is carbapenem and its group of antibiotics are observed in almost all studies. There is a strong reduction in antibiotic consumption after the ASP. A study Education of physicians, pharmacists, and patients is the tool used to make awareness regarding the benefits of judicious usage of antibiotics. In some studies, a multidisciplinary team is formed to check and teach about the different aspects of ASP which are related to antibiotic consumption, on a regular or weakly basis. An audit and feedback strategy is mostly used to do the follow-up. Consumption of antibiotics is mostly given in daily defined doses per 1000 patient days. One study provides consumption in the form of days of therapy as an interquartile range and some give percentage data to show a decreased usage of antibiotics.

In the above-given chart, the results of antibiotic consumption of seven different studies are combined and compared (1,3,5,8,10,14,15). This chart mentions the improvement in antibiotic consumption after the implementation of the antibiotic stewardship program.



Seven out of 18 studies mentioned the length of hospital stay in days and 9 studies provide information regarding the mortality rate. The result we assess in this systematic review is the decrease in length of hospital stay and mortality rate, but not much significant. Length of stay is somehow related to cost as decreased stay in hospital will preserve resources and save money.



In the above-shown chart, it can be seen that the length of hospital stays of the patients decreased after the implementation of the antibiotic stewardship program (3,6,12,14,15).

The infection of clostridium defficile is an infection that is caused by excessive exposure to the antibiotic. 2 out of 18 studies provide information regarding pseudomembranous colitis (4,18). According to studies, there is a decrease in the chances of having clostridium difficile infection after ASP.

DISCUSSION:

This systematic review of 18 recent studies from Asia Found ASPs consistently improved clinical and economic outcomes in hospitalized patients. Cost savings ranged from \$1,000 to \$12,000 per patient (1-5,7,8,10-14,18)], likely due to reduced antibiotic use and shorter

lengths of stay (3,4,6,11-15). Mortality also decreased with ASPs in most studies (1,3-5,10,12-16). The reductions in antibiotic use align with findings from systematic reviews in the US and Europe that ASPs can decrease antibiotic consumption by 22-36% (19,20).

There was some heterogeneity in study settings and methods. Most focused on adult populations and carba-penem use, while only two examined pediatric ICUs (6,9). The sustainability and long-term impacts of ASPs need further study, as most follow-up periods were less than 2 years. Additionally, the optimal personnel and interventions for ASPs in low-resource settings need to be determined.

Limitations of this review include the focus on recent studies (past 5 years) and English language articles only, which restricts generalizability. Publication bias toward positive findings may have affected results. The quality of included studies was not assessed. Out-patient and community settings were not addressed. Most studies centered on adult populations and carba-penem use, thus findings may not apply to children or overall antibiotic use. Follow-up periods were limited, with most <2 years, reducing conclusions on long-term ASP impacts. While demonstrating ASP benefits in Asia, high-quality research in broader populations and settings is still needed to optimize implementation as part of comprehensive antimicrobial stewardship globally.

CONCLUSION:

In this systematic review, it is concluded that there is a strong reduction in cost per patient in the indoor patient department. A significant amount of money can be saved after the implementation of ASP. After ASP

mortality rate decreases as well as the length of hospital stay. It helps the state economically as individual institutions to make a better policy. Patients will improve physically as well as mentally. More research work is required on: the knowledge, attitude, and practice of ASP among doctors and the community, in addition, to the education of ASP among medical personnel, community, ASP implementation in outdoor tertiary care hospitals, in primary and secondary healthcare units.

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REFERENCES:

1. Burnham JP, Olsen MA, Kollef MH. Re-estimating annual deaths due to multidrug resistant organism infections. *Infect Control Hosp Epidemiol*. 2019;40(1):112-113.
2. Singh S. Implementation and Impact of an Antimicrobial Stewardship Program at a Tertiary Care Center in South India. *Open Forum Infect Dis*. 2019; 6(4):290.
3. Zeinali Z, Muraya K, Molyneux S, Morgan R. The Use of Intersectional Analysis in Assessing Women's Leadership Progress in the Health Workforce in LMICs: A Review. *International Journal of Health Policy and Management*. 2021;11(8).
4. Mahmoudi L, Sepasian A, Firouzabadi D, Akbari A. The Impact of an Antibiotic Stewardship Program on the Consumption of Specific Antimicrobials and Their Cost Burden: A Hospital-wide Intervention. *Risk Manag Healthc Policy*. 2020; 13(1):1701-1709.
5. Honda H. Efficacy of a Post prescription Review of Broad-Spectrum Antimicrobial Agents with Feed-back: A 4-Year Experience of Antimicrobial Stewardship at a Tertiary Care Center. *Open Forum Infect Dis*. 2018; 5(12):314.
6. Haque A, Hussain K, Ibrahim R. Impact of pharmacist-led antibiotic stewardship program in a PICU of low/middle-income country. *BMJ Open Qual*. 2018;7(1):e000180.
7. Alajmi S, Almarri W. Effective Antibiotic Stewardship Program: Controlling Antibiotic Resistance and Optimizing Drug Use in Ahmadi Hospital. *J Anal Sci Methods Instrum*. 2020; 10(2):1-11.
8. Xiao Y. Change in Antibiotic Use in Secondary and Tertiary Hospitals Nationwide After a National Antimicrobial Stewardship Campaign Was Launched in China, 2011–2016: An Observational Study. *J Infect Dis*. 2020; 221 (Supplement 2):-S148-S155.
9. Murni IK, Duke T, Kinney S, Daley AJ, Laksanawati IS, Nurnaningsih, et al. Multifaceted interventions for healthcare-associated infections and rational use of antibiotics in a low-to-middle-income country: Can they be sustained? *PLoS One*. 2020; 15(6):e0234233.
10. Momattin H, Al-Ali AY, Mohammed K, Al-Tawfiq JA. Benchmarking of antibiotic usage: An adjustment to reflect antibiotic stewardship pro-

- gram outcome in a hospital in Saudi Arabia. *J Infect Public Health*. 2018; 11(3):310-313.
11. Hagiwara D, Sato K, Miyazaki M, Kamada M, Moriwaki N, Nakano T, et al. The impact of earlier intervention by an antimicrobial stewardship team for specific antimicrobials in a single weekly intervention. *Int J Infect Dis*. 2018; 77(4):34-39.
12. Haseeb A, Faidah HS, Al-Gethamy M, Iqbal MS, Barnawi AM, Elahe SS, et al. Evaluation of a Multidisciplinary Antimicrobial Stewardship Program in a Saudi Critical Care Unit: A Quasi-Experimental Study. *Front Pharmacol*. 2021;11(2):570238.
13. Hussain K, Khan MF, Ambreen G, Raza SS, Irfan S, Habib K, et al. An antibiotic stewardship program in a surgical ICU of a resource-limited country: financial impact with improved clinical outcomes. *J Pharm Policy Pract*. 2020; 13(1):69.
14. Wu CT, Chen CL, Lee HY, Chang CJ, Liu PY, Li CY, et al. Decreased antimicrobial resistance and defined daily doses after implementation of a clinical culture-guided antimicrobial stewardship program in a local hospital. *J Microbiol Immunol Infect*. 2017; 50(6):846-856.
15. Khmour MR, Hallak HO, Aldeyab MA, Nasif MA, Khalili AM, Dallashi AA, et al. Impact of antimicrobial stewardship programme on hospitalized patients at the intensive care unit: a prospective audit and feedback study. *Br J Clin Pharmacol*. 2018; 84(4):708-715.
16. Karaali C, Emiroglu M, Atalay S, Sert I, Dursun A, Kose S, et al. A new antibiotic stewardship program approach is effective on inappropriate surgical prophylaxis and discharge prescription. *J Infect Dev Ctries*. 2019;13(11):961-967.
17. Garcell HG, Arias AV, Sandoval CP, Valle Gamboa ME, Sado AB, Alfonso Serrano RN. Impact of a focused antimicrobial stewardship program in adherence to antibiotic prophylaxis and antimicrobial consumption in appendectomies. *J Infect Public Health*. 2017; 10(4):415-420.
18. Akazawa T, Kusama Y, Fukuda H, Hayakawa K, Kutsuna S, Moriyama Y, et al. Eight-Year Experience of Antimicrobial Stewardship Program and the Trend of Carbapenem Use at a Tertiary Acute-Care Hospital in Japan-The Impact of Post prescription Review and Feedback. *Open Forum Infect Dis*. 2019; 6(10):389.
19. Popovich KJ, Aureden K, Ham DC, Harris AD, Hessels AJ, Huang SS, et al. SHEA/IDSA/APIC Practice Recommendation: Strategies to prevent methicillin-resistant *Staphylococcus aureus* transmission and infection in acute-care hospitals: 2022 Update. *Infection Control & Hospital Epidemiology*. 2023;44(7):1-29.
20. Chan A, Tsang ME, Langford BJ, Nisenbaum R, Wan M, Downing MA. Evaluating a pilot, structured, face-to-face, antimicrobial stewardship, prospective audit-and-feedback program in emergency general surgery service in a community hospital. *Antimicrob Steward Healthc Epidemiol*. 2023;3(1).