



Research Article

Antimicrobial Stewardship and Prescription of Antibiotics in Healthcare Centers: A Systematic Review

Hussain Mehmood¹, Muhammad Awais², Amber Arshad³, Ammad Waheed Khan⁴, Saadia Rafique⁵, Tabinda Dugal⁶, Saira Afzal⁷,

⁽⁶⁾Consultant Royal Cornwall Hospital NHS Trust UK

⁽¹⁻⁵⁾Mayo Hospital, Lahore/King Edward Medical University Lahore, Pakistan, ⁽⁷⁾Mayo Hospital, Lahore/ King Edward Medical University Lahore, Pakistan.

Abstract:

Background: Antimicrobial resistance (AMR) is expanding rapidly worldwide. According to recent global projections, the number of fatalities will reach 4.95 million in 2019, making AMR a greater health concern than HIV or malaria alone.

Aim and Purpose: Primarily, this review is intended to understand and evaluate the global problem discussed in biomedical literature. This review seeks to synthesize the available research on antimicrobial stewardship and antibiotic prescribing.

Methodology: This study considers previous studies published between 2015 and 2022 and searches PubMed, Scopus, and Google Scholar for publications that may be relevant to the topic. Some of the search phrases used include "antimicrobial resistance," "antimicrobial stewardship," "monitoring and evaluation," "one health," and "global health." In this study, an analysis of research articles was conducted concerning antimicrobial stewardship as well as antibiotic resistance.

Findings: The previous studies have established some policies for limited resources, to improve antibiotic use and Implementation of ASPs. The studies have also highlighted the problems in the forms of inappropriate prescription and excessive antimicrobial prescribing. In addition, the researchers have proposed for a few ways to enhance antibiotic resistance and prescriptions. These strategies include basics to Resistance, the necessity to undertake frequent HCW training in antimicrobial prescription, government-oriented optimization of the infrastructure, and financial incentives.

Conclusions: The results show that ASPs have the ability to help patients use antibiotics much less, especially drugs in the WHO Watch group that have a high chance of becoming resistant. It seems sense that ASPs will aid in reducing the risk of antimicrobial resistance (AMR), given misuse and excessive use of antibiotics are two of these main causes of AMR.

Corresponding Author: Hussain Mehmood

Supervisor: Prof. Dr. Saira Afzal | Department of Community Medicine MHL/KEMU, Lahore.

Key Words: Antimicrobial resistance (AMR), prescription, systematic review, antibiotics.

INTRODUCTION:

Antimicrobial resistance (AMR) happens when bacteria, viruses, fungi, and parasites alter and stop responding to treatments. This makes it harder to cure diseases and raises the risk of disease spread, serious illness, and death. Antibiotics and other antimicrobials stop working because of drug tolerance. This makes it harder to treat infections¹.

Antimicrobial resistance, which poses a serious hazard to human, animal, and environmental health world wide, has prompted international and domestic efforts to combat the issue². The emergence of microorganisms that are resistant to antibiotics is one of the most pressing problems facing modern medicine. Despite the fact that AMR is a normal evolutionary phenomenon, the misuse or overuse of antibiotics in humans and animals continues to pose a grave threat to public health³. AMR has multiple effects on the economy, population health, environmental integrity, and social progress. Antimicrobial resistance (AMR) is responsible for severe infections, lengthier hospital stays, higher healthcare costs, an already strained public health system, higher pricing for second-line treatments, treatment failures, and even increased mortality rates⁴. Superbugs, or bacteria resistant to multiple categories of antibiotics, are an additional direct consequence of antimicrobial resistance. Antimicrobial resistance (AMR) also contributes to the declining effectiveness of antibiotics⁵⁻⁹.

The prevalence of antimicrobial resistance (AMR) is increasing globally at an alarming rate. Antimicrobial resistance poses a greater threat to public health than HIV or malaria combined, according to recent global

projections that estimate 4,95 million fatalities in 2019. If nothing is done, antimicrobial resistance could result in 10 million annual fatalities and up to \$100 trillion in annual economic losses by 2051. Antimicrobial stewardship programs (ASPs) have been implemented in a variety of settings to increase antibiotic utilization, limit the spread of resistance, ensure patient safety, and reduce wasteful healthcare spending¹⁰⁻¹⁷. Recent studies demonstrate that antimicrobial stewardship programs (ASPs) reduce antibiotic use in clinical settings by 19% overall and 27% for limited antimicrobials¹⁸. Given that the prevalence of antimicrobial resistance varies considerably across clinical settings and geographic locations, the degree to which ASPs influence antibiotic use may be influenced by the availability of resources¹⁹. Lack of reliable information regarding the efficacy of antimicrobial prophylaxes and prophylactics (ASPs) is particularly problematic in low- and middle-income countries (LMICs), where antimicrobial usage is disproportionately high compared to high income countries (HICs)²⁰.

A systematic study of antimicrobial stewardship and antibiotic prescribing in healthcare centers is done to find out how well these programs work, find out what the best practices are, and find out what might get in the way of their success. It is important to do a systematic study of antimicrobial stewardship and antibiotic prescribing in healthcare facilities if we want to learn more about how to fight AMR, improve patient outcomes, and make sure antibiotics are used in a sustainable way in healthcare settings. This study can be a helpful tool for doctors, policymakers, and other researchers who are trying to reduce the global threat

of antimicrobial resistance by putting together and analyzing the evidence we already have. Thus, this review is primarily intended to understand and evaluate the global problem discussed in biomedical literature, and then to synthesize the available research on antimicrobial stewardship and antibiotic prescribing.

MATERIALS AND METHODS:

I searched PubMed, PakMediNet and Google Scholar for articles on the topic, using terms like "antimicrobial resistance," "antimicrobial stewardship," "monitoring and evaluation," "one health," and "global health." To learn more about antimicrobial stewardship and antibiotic resistance, I read scholarly articles, editorials, comments, points of view, summaries, and white papers. Relevant data was gathered after a search was conducted of the online databases of government agencies, international trade organizations, and national trade organizations.

The article selection approach employed by the authors is depicted in Figure 1, which presents the PRISMA flow diagram. The researchers conducted a comprehensive search across three databases, including Google Scholar. We conducted a comprehensive search of three reputable medical databases (PubMed and PakMediNet), resulting in the identification of a total of 2071 articles. The authors eliminated a total of 378 duplicate records based on the initial dataset. There are a total of 1693 articles that require review. The total number of publications was reduced to 147 after conducting a thorough screening of titles and abstracts, and implementing the specified exclusion criteria. The selection of articles encompassed a specific emphasis

on the topics of antibiotic resistance and prescribing practices. Articles that were not published in the English language were also omitted from consideration. A total of 147 publications were initially retrieved for complete examination. Subsequently, 93 articles underwent thorough reading, and ultimately, 12 studies were chosen based on their adherence to the inclusion criteria.

RESULTS:

A total number of 12 studies were included because they fulfilled the review's inclusion criteria. Studies were chosen based on their use of various antibiotic stewardship strategies, including as guidelines and policies. Most of the studies found that antimicrobial stewardship improved antibiotic prescription rates. However, antimicrobial stewardship programs have been designed to have a positive economic impact by reducing unnecessary antibiotic use and preventable medical problems. In the regard of this review, antibiotic utilization patterns in hospitals and clinics were analyzed. The effect of antimicrobial stewardship on the use of antibiotics in hospitals has been analyzed. Analyses were conducted on prescription rates, antibiotic administration, and total antibiotic consumption. In light of this, the review addressed the challenges and benefits associated with antimicrobial stewardship initiatives. Challenges such as a lack of funds or supplier competition may be mentioned, as well as effective methods for overcoming them. Hence, the effectiveness of antibiotics should be preserved for future generations by prioritizing the implementation of comprehensive antimicrobial stewardship programs by healthcare institutions.

There are no free-floating parameters in this study. Since relatively few of the included studies were randomized clinical trials, we cannot conclude that ASPs cause increases in antibiotic prescription or consumption based on the pooled effect sizes. Perhaps these and other questions could be answered by keeping tabs on a control group both before and after an intervention is implemented. Antibiotic prescription patterns could shift depending on the season, weather, and other variables. Furthermore, we found that, as was previously noted, there is a dearth of research that has been conducted in LMICs. The marginal impact of a well-implemented ASP may be greater in LMICs than in HICs, although the evidence is inconclusive. The absence of information is to blame for this situation. However, we did not assess how stewardship initiatives affected animal welfare or environmental quality, two key issues from the perspective of holistic health. The previous studies have established some policies for limited resources, to improve antibiotic use and Implementation of ASPs. The studies have also highlighted the problems in the forms of inappropriate prescription and excessive antimicrobial prescribing.

Moreover, the researchers have argued some strategies to improve antimicrobial resistance and prescriptions, including essentials to Resistance, need to perform regular HCW training in antimicrobial prescription, Government-oriented optimization of the infrastructure and financial incentives.

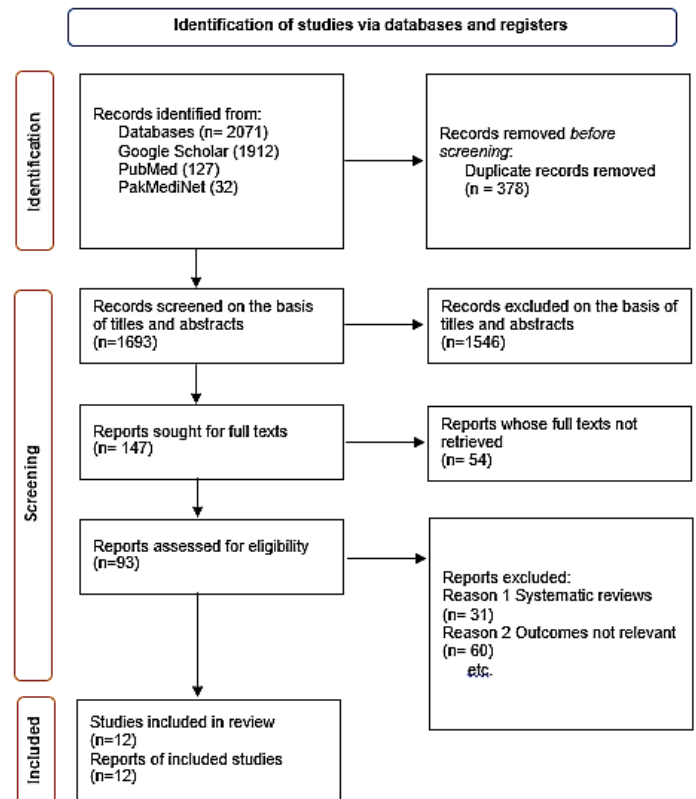


Fig. 1: PRISMA flow Diagram

Table 1: Summary of the previous studies (n=12)

Sr. No	Table 1	Title	Country	Type of Article	Outcomes
1	Cheng et al.	Antimicrobial stewardship program directed at broad-spectrum intravenous antibiotics prescription in a tertiary hospital	Australia	Original Article	For limited resources
2	Teo et al.	The effect of a whole system approach in an antimicrobial stewardship programme at the Singapore General Hospital	Singapore	Research Article	Inappropriate prescription

3	Rhee et al.	Antimicrobial stewardship in America longterm care facilities	Research Article	Essentials to Resistance
4	Majumder et al.	Antimicrobial Stewardship: Fighting Antimicrobial Resistance and Protecting Global Public Health	Peer Review	
5	Siachalinga et al	Impact of antimicrobial stewardship interventions to improve antibiotic prescribing for hospital inpatients in Africa: a systematic review and meta-analysis	Review Article	Interventions to improve antibiotic use
6	Wern Yau et al.	Antimicrobial stewardship in rural and remote primary health care: a narrative review	A Narrative Review	Inappropriate and excessive antimicrobial prescribing
7	Adegbite et al	Knowledge and perception on antimicrobial resistance and antibiotics prescribing attitude among physicians and nurses in Lambaréné region, Gabon: a call for setting-up an antimicrobial stewardship program	Original Article	Need to perform regular HCW training in antimicrobial prescription
8	Zay Ya et al.	Association Between Antimicrobial Stewardship Programs and Antibiotic Use Globally: A Systematic Review and Meta-Analysis	Review Article	ASPs are effective in reducing antibiotic consumption
9	Avent et al.	Antimicrobial stewardship in the primary care setting: from dream to reality?	Review paper	post-acute care, Strategies
10	Akpana et al.	Implementation of antimicrobial stewardship programmes in African countries: a systematic literature review	A Systematic Literature Review	Implementation of ASPs
11	Yonghong Xiao	Antimicrobial Stewardship in China: Systems, Actions and Future Strategies	Health Policy	Government-oriented optimization of the infrastructure
12	Balinskaite et al.	The Impact of a National Antimicrobial Stewardship Program on Antibiotic Prescribing in Primary Care: An Interrupted Time Series Analysis	Article	Financial incentives

DISCUSSION:

In 2008, Teo J, Kwa AL, Loh J, Chlebicki MP, and Lee W of the Divisions of General Surgery, Renal Medicine, and Endocrinology at the Singapore General Hospital began investigating antibiotic misuse. The the antibiotic, dosage, route of administration, and dura-

tion of therapy. The inspection results, which included 1535 prescriptions, were reported every three months and evaluated for an entire year. Antimicrobial stewardship programs (ASPs) were proposed as a means of resolving the issue after the study determined that improper prescribing was the leading cause of antib-

biotic resistance. Antimicrobial stewardships have been called into doubt by Charani et al., who contend that guidelines alone will not be sufficient to achieve the anticipated decrease in antibiotic resistance. To successfully reinforce improved practice, 'option architecture' is required to make smart antibiotic prescribing the path of least resistance. If we are sincere about enhancing patient outcomes and standardizing the prudent use of antibiotics throughout the healthcare industry, we must adopt a systems-based strategy. Awareness of the variables that affect antibiotic administration and prescription is the first step²¹.

Rhee et al. present a strategy for managing antimicrobial prescriptions, stating that it entails two stages in LTCFs: prior authorization and post-prescription evaluation and feedback. The objective is to prevent the future emergence of antibiotic-resistant microorganisms. Before prescribing certain antibiotics, physicians must obtain permission from a stewardship group using pre-prescription authorization. Prior authorization for prescriptions benefits all parties by minimizing the number of superfluous antimicrobials starts and maximizing the efficacy of patients' empiric antimicrobial therapy. Real-time processing could be resource- and time-intensive, delaying the beginning of treatment. This may be notably true in nursing homes and hospitals, where physicians and nurses are frequently scarce. Once additional information from clinical and microbiology laboratories becomes available, an evaluation of antimicrobial prescriptions with remarks may be conducted. It may only occur once or twice per week due to resource constraints, but its significance rests in the fact that it lasts between 48 and

72 hours. Even if it only occurs once or twice per week, it will still be beneficial. This may be simpler to achieve in LTCFs due to the increased scheduling flexibility made possible by post prescription evaluation and feedback. Since a timely evaluation of chart annotations is highly improbable, providers should be contacted via phone or encrypted email to request feedback. This study suggests that antimicrobial stewardship efforts in long-term care facilities have been successful. Therefore, these endeavors may be fruitful. At one facility, the use of oral and intravenous systemic antibiotics was reduced by 30 percent. In this study, the use of an identifying service did not prevent Monette and her colleagues from demonstrating that distributing educational materials that focus on the most prevalent ailments in LTCFs can increase antibiotic use. The prescription variation decreased by 20% after the distribution of the teaching materials²². To combat resistance and safeguard global health, Majumder et al. emphasized the significance of an antimicrobial strategy (ASP) in light of the gravity of antimicrobial resistance (AMR) and its consequences. Monitoring and evaluating adherence to antimicrobial dose regulations, promoting and preserving public health, and enhancing antimicrobial utilization were the objectives of the antimicrobial stewardship (AMS) program. How effectively the ASP employs data-driven strategies to reduce unnecessary prescriptions and overuse of antibiotics. The review indicates that the "One Health" strategy, which is both interdisciplinary and cross-sectoral, is necessary to address the growing threat posed by AMR. Antimicrobial stewardship strategies, ideas, and actions are essential for

managing and reducing antibiotic resistance. The "One Health" concept, vaccine schedules, healthcare provider training, and public awareness of antimicrobial resistance (AMR) therefore require legislation founded on research²³. Siachalinga and associates conducted this study to evaluate the effectiveness of initiatives to increase antibiotic doses for hospitalized patients. Between January 2010 and July 2022, as much investigation as possible was conducted. We reviewed any studies that examined the effect of AMS treatments on hospitalized Africans-related outcomes. The approach of the National Heart, Lung, and Blood Institute and the guidelines of the Cochrane Effective Practice and Organization of Care were used to evaluate the possibility of bias in the included studies. Using random-effects models, meta-analyses reported their findings. The overwhelming majority of studies examined were prospective and lacked control groups. Many interpreted this as evidence that improved antimicrobial management was within reach. However, additional work was required to ensure that the study's outline was accurate and useful²⁴.

By conducting this narrative review, Jun Wern Yau and colleagues hope to answer several questions regarding antibiotic prescribing and use, such as: what factors increase the likelihood of inappropriate use or prescribing; how antibiotic prescribing and use contribute to the development of antimicrobial resistance; and how effective antimicrobial stewardship strategies are in primary health care facilities located in rural and remote areas. The entire global output of written English between 2000 and 2020 was located using keywords. Relevant data was extracted from seven

distinct online sources. These resources included Scopus, Cochrane, Embase, CINAHL, PubMed, Ovid Medline, and Ovid Emcare. The systematic review procedures of the Joanna Briggs Institute were utilized to investigate and evaluate the studies. Antibiotics that are administered excessively or unnecessarily result in the development of resistant microorganisms. This is particularly true for primary care clinics serving rural and remote communities. Antimicrobial stewardship programs, such as education, clinical assistance, surveillance, and legislation, have reduced the quantity and frequency of unnecessary prescriptions. In the narrative review, the significance of monitoring antibiotic resistance during prolonged treatment was emphasized at length. There were no significant differences in health status between urban and suburban controls. Adegbite et al. 27 interviewed HCW at the regional referral hospital, a medical research facility, and tertiary care facilities using self-administered questionnaires. Using Fisher's Exact test, the number of correct responses from physicians and nurses was compared. 47 healthcare workers responded. 64% of Gabonans surveyed (30/47) viewed antibiotic resistance as a serious threat to public health, whereas only 30% (14/47) viewed it as a major concern where they presently worked. The majority of respondents (37 out of 47) believe that improper antibiotic use and the use of over-the-counter drugs contribute to the spread of antibiotic resistance. One-fifth (32%) of physicians believed antibiotics accelerated recovery in patients with malaria when combined with other treatments, and 28% (13/47) reported prescribing antibiotics to patients who requested them. More physicians (95%;

18/19) and nurses (68%) believe that AMR is spread when antibiotics are prescribed without first using a microscope to corroborate the diagnosis. The vast majority of physicians and scientists surveyed believe that AMR poses a significant threat to public health. However, more than 25% of those surveyed were unable to articulate what causes antibiotics to be weakened. Programs for the responsible use of antibiotics should be established, and health care professionals should receive regular training on the safe and effective administration of antibiotics²⁵.

Researchers Zay Ya et al. combed PubMed, Web of Science, and Scopus for articles published between August 1, 2010, and August 1, 2020, that examined the relationship between antimicrobial stewardship activities and global antibiotic consumption. By examining the cited references of the systematic studies that we had already utilized, we were able to incorporate additional papers. As recommended by the Preferred Reporting Items in Systematic Reviews and Meta-Analyses guideline, antimicrobial use and specific ASPs were evaluated using multilevel random-effects models. Utilizing a method devised for the Effective Public Health Practice Project, the quality of the works was determined. In total, 52 studies (1 794 889) investigated the relationship between antibiotics and ASPs. Forty of the investigations were conducted in countries with high incomes, while the remaining twelve were conducted in developing nations. When ASPs were used, antimicrobial use decreased by 28% (rate ratio of 0.72) and antibiotic concentrations decreased by 10% (CI range of 4% to 15%). In hospitals with ASPs, antimicrobial use decreased 21%

(95% CI, 5%-36%), whereas it increased 28% (rate ratio, 0.72; 95% CI, 0.56-0.92) in hospitals without ASPs. This systematic review and meta-analysis of ASPs demonstrates their effectiveness in reducing antibiotic overuse in hospital and outpatient clinic settings. Due to a paucity of data, we are unable to determine whether or not ASPs are effective in low-resource environments²⁶.

As in hospitals and nursing homes, Avent et al. contend that longer-term financial, behavioral, and regulatory variables can encourage the use of AMS programs in primary care. Without these safeguards, antimicrobial stewardship (AMS) programs and community efforts to reduce unnecessary antibiotic use would be widely rejected. Before AMS can be implemented in primary care across an entire community, according to the authors, a centralized strategy involving multiple strategies to assist practitioners and obtain clearance is required. They advocate for a national accreditation standard for the Core Elements of Outpatient Antibiotic Stewardship and additional funding to improve the quality of AMS care. In this article, numerous methods are discussed. A community-accepted AMS treatment plan necessitates a top-down strategy that incorporates commitment from the bottom up with multiple approaches. The criteria for approval are based on the Core Elements of Outpatient Antibiotic Stewardship. This strategy can only be implemented if there is sufficient funding for the interventions involved in quality improvement initiatives. If these conditions are not met, programs that rely on AMS to reduce antibiotic overuse in the community will fail²⁷. Akpana et al. were primarily interested in determining

the current status of ASPs in Africa and their effects. For this investigation, we searched PubMed, Scopus, the Cochrane Library, African Journal Online, CINAHL, and Google Scholar for peer-reviewed articles published between 1990 and March 2019. They combined the names of the five African regions with antimicrobial stewardship-related nouns and adjectives. As a viable research methodology, any theory or management framework has been suggested. Using the NHLBI's method for grading the quality of before-and-after investigations, the aggregate quality of the included studies was assessed. Only 13 out of 1,752 results were deemed suitable for further investigation. South Africa was subjected to seven evaluations, whereas Sudan, Tanzania, and Egypt were each subjected to only one. Overall, the quality and consistency of the eleven studies was quite exceptional. In the reviewed studies, process metrics were found to increase adherence to antibiotic stewardship recommendations, decrease the number of incorrect prescriptions, reduce antibiotic use, and save money. Despite a reduction in surgical site infections, there were no statistically significant differences between the two groups in the 30-day readmission or mortality rates. This study demonstrates how little is known about the implementation of ASPs in African nations. The successes of the included studies indicate that additional African nations can implement comparable programs despite the obstacles that make it difficult to deploy ASPs effectively²⁸. According to Yonghong Xiao, antimicrobial resistance (AMR) is common in China. China has developed an Antimicrobial Stewardship Management System and Technical Support

Framework over the past decade. Patient outcomes have vastly improved as a result of the department of health's initiatives to increase the appropriate clinical use of antibiotics in hospitals. The appropriate use of antibiotics has improved, but more can be done to reduce unnecessary prescriptions. Long-term AMR management calls for a two-person, two-pronged approach. This strategy requires the establishment of a system and infrastructure for rational antibiotic use and AMR control, as well as the formation of expert teams, to assure the long-term viability of AMR control. In addition, the plan emphasizes the significance of government leadership during this transition. After contemplating the causes of antimicrobial resistance (AMR), such as the structure of China's healthcare system and the need for long-term efforts to reduce AMR, he concludes that the "two steps and two hands" strategy is necessary. The government must exert substantial pressure on the general public to employ antimicrobial agents responsibly. Accurate AMR control is one of the many responsibilities that will necessitate consistent attention from trained personnel throughout the remainder of the year. Thus, the "firsthand" reference. The term "second hand" is used to describe the method of assembling specialist teams in order to devise strategies for the long-term management of AMR²⁹.

Between April 2013 and February 2017, researchers Violeta Balinskaite and colleagues examined a national antibiotic prescribing dataset in order to determine the total number of antibiotic items prescribed per STAR-PU, the number of broad-spectrum antibiotic items prescribed, and the percentage of broad-

spectrum antibiotic items prescribed. The impact of the Quality Premium was determined by segmented regression analysis of interrupted time series data on antibiotic usage trends. During the research period, nearly 140 million antibiotic prescriptions were written by primary care physicians. In the 23 months following the implementation of the Quality Premium, prescriptions for antibiotics decreased by 8.2%. This is a decrease of 5,933,563 antibiotic prescriptions compared to what would have been expected given the trend from the previous year. When age and gender differences were accounted for by a segmented regression model, the total amount of antibiotic products supplied to all STAR-PUs decreased significantly. During the same time frame, there was a decrease of 18.9% in the number of prescriptions written for broad-spectrum antibiotics, which account for only 10.1% of all medications. Researchers discovered that by providing financial incentives to local healthcare commissioners in England, antibiotic prescribing overall and broad-spectrum antibiotic prescribing decreased significantly³⁰.

CONCLUSION:

This in-depth study found that antimicrobial stewardship programs (ASPs) are tied to a drop in the number of antibiotic prescriptions in hospitals. The results show that ASPs have the ability to help patients use antibiotics much less, especially drugs in the WHO Watch group that have a high chance of becoming resistant. Since overusing and misusing antibiotics are two of the main reasons for antimicrobial resistance (AMR), it makes sense that ASPs will help reduce this danger.

ACKNOWLEDGMENTS:

We would like to express our sincere gratitude and appreciation to Dr. Tabinda Dugal, Dr. Saira Afzal for their unwavering support and assistance in this research work. Their valuable guidance and input have been instrumental in ensuring the success of our publication. We are truly grateful for their contributions.

REFERENCES:

1. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *The Lancet infectious diseases*. 2010;10(9):597-602.
2. Ahmed D, Javed H, Kanwal W, Fatima W, Qadir NA. Determination of Multidrug Resistance and Extended Drug Resistance Pattern of *Pseudomonas aeruginosa* in Clinical Isolates of Tertiary Care Hospital Lahore. *Annals of King Edward Medical University*. 2023;29(2):98-104.
3. McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA*. 1995;273(3):214-9.
4. Sintchenko V, Coiera E, Gilbert GL. Decision support systems for antibiotic prescribing. *Current opinion in infectious diseases*. 2008;21(6):573-9.
5. Carling P, Fung T, Killion A, Terrin N, Barza M. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. *Infection Control & Hospital Epidemiology*. 2003;24(9):699-706.

6. De Man P, Verhoeven BA, Verbrugh HA, Vos MC, Van den Anker JN. An antibiotic policy to prevent emergence of resistant bacilli. *The Lancet*. 2000;355(9208):973-8.
7. Buchy P, Ascioğlu S, Buisson Y, Datta S, Nissen M, Tambyah PA, et al. Impact of vaccines on antimicrobial resistance. *International Journal of Infectious Diseases*. 2020; 90(1):188-96.
8. Fowler S, Webber A, Cooper BS, Phimister A, Price K, Carter Y, et al. Successful use of feedback to improve antibiotic prescribing and reduce *Clostridium difficile* infection: a controlled interrupted time series. *Journal of Antimicrobial Chemotherapy*. 2007;59(5):990-5.
9. Thaler RH, Sunstein CR. *Nudge: improving decisions about health. Wealth and Happiness*. 2008; 6(1):14-38.
10. Lewis PJ, Tully MP. Uncomfortable prescribing decisions in hospitals: the impact of teamwork. *Journal of the Royal Society of Medicine*. 2009;102(11):481-8.
11. Dunagan WC, Woodward RS, Medoff G, Gray III JL, Casabar E, Smith MD, et al. Antimicrobial misuse in patients with positive blood cultures. *The American journal of medicine*. 1989;87(3):253-9.
12. Fortini A, Faraone A, Di Pietro M, Cappugi C, Magnante G, Boccadori C, et al. Antimicrobial stewardship in an Internal Medicine ward: effects on antibiotic consumption and on the use of carbapenems. *Internal and Emergency Medicine*. 2018;13(8):1219-26.
13. Afzal MF. Antibiotic stewardship: battle to defeat superbugs. *Annals of King Edward Medical University*. 2017;23(2):97.
14. Tedeschi S, Trapani F, Giannella M, Cristini F, Tumietto F, Bartoletti M, et al. An antimicrobial stewardship program based on systematic infectious disease consultation in a rehabilitation facility. *Infection control & hospital epidemiology*. 2017;38(1):76-82.
15. Gerber JS, Prasad PA, Fiks AG, Localio AR, Grundmeier RW, Bell LM, et al. Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians: a randomized trial. *JAMA*. 2017;309(22):2345-52.
16. Kasset N, Sham R, Aleong R, Yang D, Kirzner M, Craft A. Impact of antimicrobial stewardship on physician practice in a geriatric facility. *The Canadian Journal of Hospital Pharmacy*. 2016;69(6):460.
17. Khdour 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. *British journal of clinical pharmacology*. 2018;84(4):708-15.
18. Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E. Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs. *Antimicrobial agents and chemotherapy*. 2016;60(8):4840-52.
19. Anwar A, Faisal R, Mahmood A, Naz H, Sibtain SA, Shinwari L. Antibiotic use in infants: a cross-

- sectional survey assessing the knowledge, attitudes and practices of health professionals. *Annals of King Edward Medical University*. 2017;23(3):371-75.
20. Alsan M, Schoemaker L, Eggleston K, Kammili N, Kolli P, Bhattacharya J. Out-of-pocket health expenditures and antimicrobial resistance in low-income and middle-income countries: an economic analysis. *The Lancet infectious diseases*. 2015;15(10):1203-1210.
21. Cheng VC, To KK, Li IW, Tang BS, Chan JF, Kwan S, et al. Antimicrobial stewardship program directed at broad-spectrum intravenous antibiotics prescription in a tertiary hospital. *European journal of clinical microbiology & infectious diseases*. 2009;28(12):1447-56.
22. Teo J, Kwa AL, Loh J, Chlebicki MP, Lee W. The effect of a whole-system approach in an antimicrobial stewardship programme at the Singapore General Hospital. *European journal of clinical microbiology & infectious diseases*. 2012;31(1):947-55.
23. Rhee SM, Stone ND. Antimicrobial stewardship in long-term care facilities. *Infectious Disease Clinics*. 2014;28(2):237-46.
24. Majumder MA, Rahman S, Cohall D, Bharatha A, Singh K, Haque M, et al. Antimicrobial stewardship: Fighting antimicrobial resistance and protecting global public health. *Infection and drug resistance*. 2020;13(1):4713-38.
25. Ali II, Khan IA, Munir MK, Rasool SA. Current pattern of antibiotic resistance in clinical isolates of *Acinetobacter baumannii* from intensive care units of tertiary care hospital. *Annals of King Edward Medical University*. 2016;22(1):17-22.
26. Yau JW, Thor SM, Tsai D, Speare T, Rissel C. Antimicrobial stewardship in rural and remote primary health care: a narrative review. *Antimicrobial Resistance & Infection Control*. 2021;10(1):1-33.
27. Farooka MW, Khan WH, Parvez H, Ayyaz M. Role of antibiotic prophylaxis in clean and clean contaminated elective surgery. *Annals of King Edward Medical University*. 2005;11(4):589-91..
28. Avent ML, Cosgrove SE, Price-Haywood EG, Van Driel ML. Antimicrobial stewardship in the primary care setting: from dream to reality?. *BMC family practice*. 2020; 21(1):1-9.
29. Xiao Y. Antimicrobial stewardship in China: systems, actions and future strategies. *Clinical Infectious Diseases*. 2018; 67(1):135-141.
30. Balinskaite V, Johnson AP, Holmes A, Aylin P. The impact of a national antimicrobial stewardship program on antibiotic prescribing in primary care: an interrupted time series analysis. *Clinical Infectious Diseases*. 2019;69(2):227-32.