Review Article

Antimicrobial Stewardship Programme (ASP): Is Prospective Audit and Feedback an Effective Strategy to Reduce Irrational Antibiotic Use?

Rifana KM[1], Shafeeque Rahman CP[1], Shuhaila Muhammad Ali[1], Dr.Linu Mohan P[2]

1. Mpharm Pharmacy Practice Student, Alshifa College of Pharmacy, Perinthalmanna, Malappuram district, Kerala, India.
2. Professor, Department of Pharmacy Practice, Alshifa College of Pharmacy, Perinthalmanna, Malappuram district, Kerala, India.

***Corresponding author's E-mail:** rifanakm97@gmail.com

Received: 18-02-2023; **Revised:** 26-04-2023; **Accepted:** 05-05-2023; **Published on:** 15-05-2023.

ABSTRACT

Antibiotic stewardship is a developing programme that implemented in many countries which increased the rational use of antibiotic in infected population. Since antibiotics are one of the large categories which frequently prescribed by physicians, The importance of Antimicrobial stewardship programs have been increased in this era, because it shown to improve patient outcomes, shorten length of stay, reduce antibiotic resistance, and save money in the inpatient setting. Among the different core elements, the prospective audit and feedback method is used in many of institutions and countries. By reviewing many studies, it concluded that prospective audit and feedback method is effective to reduce irrational antibiotic prescribing. The feedback given to the physician generally are stop antibiotic, IV to oral change, dose optimization etc. Few studies also showed that ASP reduce the cost of antibiotic therapy.

Keywords: Antimicrobial stewardship programme (ASP), Prospective audit and feedback, Inappropriate antibiotic use, Pharmacist intervention.

QUICK RESPONSE CODE →

DOI: 10.47583/ijpsrr.2023.v80i01.020

DOI link: http://dx.doi.org/10.47583/ijpsrr.2023.v80i01.020

INTRODUCTION

Antibiotic stewardship is defined as any activity that promote selection of optimal dosing, route of administration and duration of therapy for antibiotics[1]. Antimicrobial stewardship programs (ASP) are one of the interventions that have been proved to reduce antimicrobial use (AU) in children[2]. Since antibiotics are one of the large category which frequently prescribed by physicians. The importance of Antimicrobial stewardship programs have been increased in this era, because it shown to improve patient outcomes, shorten length of stay, reduce antibiotic resistance, and save money in the inpatient setting[3]. Implementing an antimicrobial stewardship program (ASP) is one strategy to help curb the inappropriate use of antimicrobials and, in turn, decrease resistance associated with misuse[4]. The emergence of antibiotic-resistant organisms and the lack of development of new antimicrobials have made it imperative that additional strategies be developed to maintain the effectiveness of these existing antibiotics[5]. Antimicrobial stewardship interventions are increasingly being advocated as an important strategy to increase the appropriateness of antimicrobial prescribing, with the aim of preventing or delaying the emergence of resistance[6]. Children are highly vulnerable patient population, as it considers that they are the future of the world and the inappropriate antibiotic therapy leads to antibiotic resistance in children that causes a flaw on the health of coming population. The importance of antibiotic stewardship increasing day by day in whole world since the emerging growth of antibiotic resistance is unimaginably high while the development and marketing of new antibiotics are in slow rate. The introduction of antibiotic therapy in children is difficult, because results are not ready before necessary decision on initiation of antibiotics. As laboratory tests may be unspecific and delayed, and clinical signs can be prone to subjective interpretation, risk assessment is often used, with a low threshold for starting empiric antibiotic therapy[7]. Reductions in antibiotic consumption have historically had variable impacts on resistance levels, likely dependent on setting, baseline consumption and resistance patterns, and fitness costs[8]. This review article discussed about the antibiotic stewardship strategy -prospective audit and feedback, how effectively it reduces inappropriate antibiotic use among people particularly in paediatric population.

DISCUSSION

The Antibiotic stewardship implementation improves the rational use of antibiotic among paediatric population. The studies on this topic described various aspects of the antibiotic use. A pre-post study, comparing systemic Antibiotic use and Length of stay in paediatric inpatients admitted for Appendix Related-Intra abdominal Infections after the implementation of an Antibiotic Stewardship Programme (ASP) based on Post prescription review with feedback. They found that Surgery departments have been identified as those that may benefit the most from ASP because of prescriptions including unnecessary prolonged

antibiotic regimens and unnecessary use of wide-spectrum antibiotics, both in adult and paediatric patients. This study analysed the impact of the first 3 years of a paediatric ASP based on post-prescription review with feedback (PPRF) on Antibiotic use, Length of stay, and Quality of prescription in children and adolescents with Appendix Related-Intra Abdominal Infections. The intervention significantly reduced Length of stay and Length of therapy in phlegmonous appendicitis, but not in the rest of diagnoses. Piperacillin–tazobactam use dramatically decreased without any rebound in the use of carbapenems or other wide-spectrum antibacterials, did not observe changes in global Antibiotic use in the postintervention period. study is limited by the observational design, the short follow-up time, Additionally, no data on antimicrobials prescribed at discharge were recorded. They were unable to assess the financial results of intervention group[2]. While another study which is conducted in Norway explained that antibiotic exposure in-hospital was associated with an almost three times increased risk of antibiotic exposure and a more than six times increased incidence rate of total antibiotic prescriptions in ambulatory care both during the year before and the year after hospitalisation. In the H+ group that is group which got antibiotic in-hospital, they observed a trend towards more ambulatory antibiotic exposures in girls versus boys both before and after hospitalisation. strength of this study is that they used prospectively collected clinical data in combination with national registry data. One limitation of the study is that comorbidity status in the two groups were obtained by two different methods. Despite this, it was regarded that approach most accurate with the purpose to include a wide range of chronical conditions[9].

A retrospective study on appropriateness of antibiotic prescribing in hospitalized children were performed in Italy. The results showed the occurrence of a high rate of antibiotic inappropriate prescription; more than half of the prescribed antibiotics was inappropriate. The emergency paediatrics unit showed the higher rate of inappropriate antibiotic prescribing. The present data confirm that the availability of “a paediatric emergency unit” does not cause any improvement in the appropriateness of antibiotic therapy and in the selection of the right antibiotic, likely as a consequence of the need to treat patients for a fast clinical evaluation without any in-depth further analysis of the clinical status. ceftriaxone and clarithromycin were the most inappropriate molecules. this Australian survey showed that older age was significantly associated with inappropriate prescribing. ceftriaxone was the active ingredient with the highest prevalence of use, followed by amoxicillin and clavulanic acid. The main limitation of the study were this is a single-centre study and enrolled patients were only hospitalized[10]. It is identified that the impact of short course antimicrobial therapy for paediatric community acquired pneumonia is equivalent to the standard 10 days antibiotic therapy .The study was performed in Eastern Ontario where the implementation ASP improved SAFER therapy (short course antimicrobial therapy for paediatric respiratory infection[11]. A study conducted to prove that implementation of pharmacist interventions improves compliance to community acquired pneumonia (CAP) guidelines. This pharmacist-driven, antibiotic stewardship implementation study measuring compliance to a CAP guideline bundle in both public- and private-sector hospitals showed an overall improvement in both diagnostic and antibiotic measures[12]. Antimicrobial stewardship strategy that is audit and feedback method in corona virus infected patients is implemented in a study in South India. The sample was categorized as mild and moderate to severe according to the severity of viral infection. Among the antibiotic classes, there was a significant reduction in usage of beta-lactams in both mild and moderate-to- severe categories. The length of hospital stay did not change significantly in the moderate-to-severe category, but reduced significantly in the mild category. focus group discussion and regular feedback audit can successfully reduce antibiotic overuse in these patients without adversely affecting clinical outcomes like length of stay and mortality[13].

Katherine Goodman et al stated that antimicrobial Prospective audit and feedback (PAF) with statistical and machine learning approach will improve rational use of antibiotic, found that many clinical and antimicrobial characteristics were significantly associated with PAF intervention; these variables may help identity targets for increasing antibiotic order appropriateness. presence of a clinical pharmacist on the ordering unit or receipt of an ID consult were associated reduced inappropriate antibiotic use. Hence machine learning classifier helped to reduce the reviews[14]. A retrospective study on the implementation of antimicrobial stewardship by a clinical pharmacist conducted in a Chinese hospital showed the proportion of antibiotic prescriptions in outpatients and inpatients declined in each month during the intervention stage. The proportion of antibiotic prophylaxis in patients undergoing type I incision operations was significantly reduced. They predicted that the global mortality attributable to Antimicrobial resistance (AMR) is estimated to reach 10million annually by 2050, which would make it one of the leading causes of death, with an economic impact of up to US$100 trillion. The results showed that with decreased intensity of Fluoroquinolones (FQs) consumption, the resistance rates of E. coli and P. aeruginosa to FQs and incidence rate of Methicillin resistant *Staphylococcus aureus* (MRSA) showed decreasing trends, and they were positively correlated. The findings of study indicate some directions to pursue in controlling the prevalence of carbapenem-resistant Enterobacteriaceae (CRE) and Methicillin Resistant *Staphylococcus aureus*[15].

An interventional study by prospective audit and feedback for implementing antimicrobial stewardship programme in a Norwegian hospital increased the adherence to the guidelines. By implementing AMS the mean duration of antibiotic therapy reduced and achieved a 10 percentage-

point targeted reduction in prescribing of high-dose benzylpenicillin. Thus substantially reduced prescribing of broad-spectrum antibiotics known to promote AMR, and succeeded in reducing prescribing of these antibiotics with no obvious negative effect on measured clinical outcomes. strength in the study is that the physicians at the study department were not informed about the pre-intervention audit before they presented the audit results. Consequently, Hawthorne effects can be ruled out. Results indicate that Audit &Feedback is suitable for reducing prescribing of broad- spectrum antibiotics, and the design can potentially be expanded to other low Antimicrobial Resistance-settings[16]. AMS in Pneumonia patients performed by Audit and feedback focused approach for evidence based care in treatment (AFFECT Study) increased adherence to local best practice and resulted in a nonsignificant trend toward reduced duration of treatment. Oral amoxicillin– clavulanate was recommended over oral cefuroxime because of its better oral bioavailability and lower cost. IV ceftriaxone, a third-generation cephalosporin, was preferred over IV cefuroxime on the basis of its increased coverage of Streptococcus pneumoniae, as well as broader coverage of gram-negative organisms. Major changes from the pre-intervention audit to the post-intervention audit were increases in the prescribing of amoxicillin-clavulanate and azithromycin and reductions in use of levofloxacin and moxifloxacin, changes that are consistent with the treatment algorithm recommendations. There were no significant changes in the duration of IV, oral, or total treatment, except for oral therapy in Health Care Associated Pneumonia patients, which significantly decreased[17].

The prospective audit and feedback (PAAF) method improved the total antibiotic use in the hospital in order to evaluate the antibiotic use in every day. They performed auditing of prescriptions in the surgical, respiratory, and medical wards. The appropriate recommendations for improving rational use were given to the physicians and acceptance and rejection were recorded. The most common recommendations made over the study period included optimizing the duration of antibiotic therapy, recommendations to discontinue antibiotic therapy, and changes in the route of administration. On the surgical wards, total antibiotic use decreased from 765 Days of therapy (DOTs) per 1,000 patient days in the baseline period to 572 DOTs per 1,000 patient days after PAAF initiation. The results of the interrupted time series model demonstrated that although total systemic antibiotic use showed a non-significant declining trend before the introduction of PAAF, antibiotic use was significantly decreased by 100 DOTs per 1,000 patient days immediately after intervention implementation, signifying a 12% reduction. In the surgical words amoxicillin/clavulanic acid, cefazolin, and ceftriaxone showed decreases in utilization during the intervention period. In respiratory ward small increases in utilization were observed for amoxicillin, amoxicillin/ clavulanic acid, ampicillin, azithromycin, cefazolin, ceftazidime, and cephalexin. This is one of the main study were cost of antibiotic therapy assessed. On the surgical wards, daily antibiotic costs were reduced by 35% after the introduction of antimicrobial stewardship. Costs decreased 41% on the respiratory ward, on the medical wards, antibiotic costs declined by 35%[18]. Antibiotic stewardship has different components, The results of this study represent a formal comparison of the 2 core antimicrobial stewardship- prior authorization and prospective audit and feedback methods within a single institution. The findings of the study suggested that findings the change from prior authorization to prospective audit with feedback was associated with a significant increase both in use of the affected antimicrobials and in overall use of all antimicrobial agents. On comparing the pre and post intervention period, the consumption of broad spectrum gram negative antimicrobial and length of the antibiotic therapy decreased[19].

Antibiotic prescribing trends before and after implementation of an audit and feedback program in internal ward of a tertiary hospital in Tehran was assessed in a study which showed reduced discrepancy from guidelines and led to more appropriate treatment without any detrimental effect on treatment outcomes. Intervention was reduced hospital stay significantly with no effect on mortality rate. Physicians in this study accepted 81% of recommendations. post prescription review of IV antibiotics and feedback is an effective intervention to increase appropriateness of the treatment and to reduce the broad-spectrum antibiotic usage. This research has also demonstrated that this intervention could decrease the hospital length of stay with no effect on mortality[20]. Combined influence of implementing practice guidelines and prospective audit and feedback of prescription as stewardship on antimicrobial treatment of community-acquired pneumonia (CAP) and empyema in children were showed a decrease in the use of second and third-generation cephalosporins, and a corresponding increase in the use of Amino penicillins in the treatment of CAP in hospitalized, healthy, primarily immunized children, including those with empyema. The mean length of stay not changed during 5 year study duration. They implemented American and Canadian guidelines for prescribing of antibiotic for community acquired pneumonia and compliance of physician prescribing with these guidelines were compared. compliance with penicillin as first- line therapy in inpatients was 55% while broad-spectrum antimicrobials were 27%. A post guideline survey of treatment of uncomplicated CAP concluded that guidelines and education resulted in only modest improvements in prescribing practices and additional strategies are required. The combined effects resulted in 63% of the patients receiving empiric ampicillin treatment with a significant decrease in ceftriaxone use. children who had viruses detected had a shorter duration of discharge antimicrobials compared to those who did not, there was

no difference in in-hospital day of therapy between the two groups. The study provided additional evidence that narrow-spectrum agents such as Amino penicillins do not prolong hospital stay nor lead to increased complications, even in patients with empyema. Community acquired Pneumonia guidelines were successful in decreasing the use of cephalosporins in favour of ampicillin, and Antimicrobial Stewardship rounds likely provided incremental value in reinforcing the need to avoid broader-spectrum cephalosporins and decreasing the duration of post discharge antimicrobials[21].

Acute bronchitis remains a common diagnosis where antibiotics are prescribed despite being a predominately viral illness. Guidelines and evidence-based practices advise against antibiotics for this diagnosis. The decision to prescribe antibiotics is complex and driven by several interdependent factors, such as patient expectations, health system limitations, clinician training, and specialty. Antibiotic prescribing rates decreased from 75% at baseline to 60% at post education month. Limitation of the study was study did not account for the duration of symptoms as a factor to judge appropriateness. Study findings showed a decline in potentially inappropriate antibiotic prescribing for viral infection and a resulting improvement in clinical antimicrobial stewardship efforts[22].Another study implemented antibiotic stewardship audit and feedback mainly focusing on IV to oral switch, thus reduce the length of inpatient hospital admission. median duration of total intravenous therapy significantly decreased from 62 hours 45min pre-implementation to 48 hours. The median length of inpatient hospital admission correspondingly decreased from 78 hours pre-implementation to 63 hours 51min, representing approximately 14 hours' reduction in both measures. Many studies are conducted with the aim to reduce antibiotic use and cost of therapy etc, but this study address inappropriately long intravenous antibiotic durations in multiple conditions affecting hospitalised children[23].

CONCLUSION

The antimicrobial stewardship programme is one of the best implemented programme to reduce inappropriate antibiotic use among population. There are many strategies implemented for the ASP like prior authorization, Formulary restriction, prospective audit and feedback and antimicrobial order forms etc. Prior studies of stewardship interventions have found implementation prospective audit with feedback to be effective strategy for decreasing antimicrobial exposure, decreasing costs, and improving clinical outcomes. The ASP was associated with an immediate and sustained decrease in targeted antibiotic consumption as well as in overall antibiotic use. The prospective audit and feedback help to check the appropriateness of antibiotic therapy for patient conditions and provide recommendations to improve rational antibiotic use, which helps the healthcare professionals to improve the therapy and also their education. The recommendations generally include stop antibiotics, IV to Oral change of antibiotic, de-escalation of dose, dose optimization etc. All these recommendations help to improve rational use of antibiotic. The co-implementation of two AP strategies at a site like PAF with Prior authorization or formulary restriction etc, will enhance impact of the therapy.

REFERENCES

1. Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: a WHO practical toolkit. JAC-Antimicrob Resist. 2019 Dec 1;1(3):dlz072.

2. Simó S, Velasco-Arnaiz E, Ríos-Barnés M, López-Ramos MG, Monsonís M, Urrea-Ayala M, et al. Effects of a Paediatric Antimicrobial Stewardship Program on Antimicrobial Use and Quality of Prescriptions in Patients with Appendix-Related Intraabdominal Infections. Antibiotics. 2020 Dec 23;10(1):5.

3. Szymczak JE, Feemster KA, Zaoutis TE, Gerber JS. Pediatrician Perceptions of an Outpatient Antimicrobial Stewardship Intervention. Infect Control Hosp Epidemiol. 2014 Oct;35(S3):S69–78.

4. Klatte JM. Pediatric Antimicrobial Stewardship Programs: Current Perspectives. Pediatr Health Med Ther. 2020 Jul;Volume 11:245–55.

5. Newland JG, Stach LM, De Lurgio SA, Hedican E, Yu D, Herigon JC, et al. Impact of a Prospective-Audit-With-Feedback Antimicrobial Stewardship Program at a Children's Hospital. J Pediatr Infect Dis Soc. 2012 Sep;1(3):179–86.

6. Taggart LR, Leung E, Muller MP, Matukas LM, Daneman N. Differential outcome of an antimicrobial stewardship audit and feedback program in two intensive care units: a controlled interrupted time series study. BMC Infect Dis. 2015 Dec;15(1):480.

7. Rajar P, Saugstad OD, Berild D, Dutta A, Greisen G, Lausten-Thomsen U, et al. Antibiotic Stewardship in Premature Infants: A Systematic Review. Neonatology. 2020;117(6):673–86.

8. Tedijanto C, Grad YH, Lipsitch M. Potential impact of outpatient stewardship interventions on antibiotic exposures of common bacterial pathogens. eLife. 2020 Feb 5;9:e52307.

9. Thaulow CM, Blix HS, Nilsen RM, Eriksen BH, Wathne JS, Berild D, et al. Antibiotic use in children before, during and after hospitalisation. Pharmacoepidemiol Drug Saf. 2022 Jul;31(7):749–57.

10. Nasso C, Scarfone A, Pirrotta I, Rottura M, Giorgi DA, Pallio G, et al. Appropriateness of Antibiotic Prescribing in Hospitalized Children: A Focus on the Real-World Scenario of the Different Paediatric Subspecialties. Front Pharmacol. 2022 May 26;13:890398.

11. Pernica JM, Harman S, Kam AJ, Carciumaru R, Vanniyasingam T, Crawford T, et al. Short-Course Antimicrobial Therapy for Pediatric Community-Acquired Pneumonia: The SAFER Randomized Clinical Trial. JAMA Pediatr. 2021 May 1;175(5):475.

12. van den Bergh D, Messina AP, Goff DA, van Jaarsveld A, Coetzee R, de Wet Y, et al. A pharmacist-led prospective antibiotic stewardship intervention improves compliance to community-acquired pneumonia guidelines in 39 public and

private hospitals across South Africa. Int J Antimicrob Agents. 2020 Dec;56(6):106189.

13. Borde K, Medisetty MK, Muppala BS, Reddy AB, Nosina S, Dass MS, et al. Impact of an Antimicrobial Stewardship Intervention on Usage of Antibiotics in Coronavirus Disease-2019 at a Tertiary Care Teaching Hospital in India. IJID Reg. 2022 Jun;3:15–20.

14. Goodman KE, Heil EL, Claeys KC, Banoub M, Bork JT. Real-world Antimicrobial Stewardship Experience in a Large Academic Medical Center: Using Statistical and Machine Learning Approaches to Identify Intervention "Hotspots" in an Antibiotic Audit and Feedback Program. Open Forum Infect Dis. 2022 Jul 4;9(7):ofac289.

15. Wang H, Wang H, Yu X, Zhou H, Li B, Chen G, et al. Impact of antimicrobial stewardship managed by clinical pharmacists on antibiotic use and drug resistance in a Chinese hospital, 2010–2016: a retrospective observational study. BMJ Open. 2019 Aug;9(8):e026072.

16. Høgli JU, Garcia BH, Skjold F, Skogen V, Småbrekke L. An audit and feedback intervention study increased adherence to antibiotic prescribing guidelines at a Norwegian hospital. BMC Infect Dis. 2016 Dec;16(1):96.

17. Halpape K, Sulz L, Schuster B, Taylor R. Audit and Feedback-Focused approach to Evidence-based Care in Treating patients with pneumonia in hospital (AFFECT Study). Can J Hosp Pharm [Internet]. 2014 Mar 6 [cited 2023 Apr 5];67(1). Available from: http://www.cjhp-online.ca/index.php/cjhp/article/view/1317

18. Campbell TJ, Decloe M, Gill S, Ho G, McCready J, Powis J. Every antibiotic, every day: Maximizing the impact of prospective audit and feedback on total antibiotic use. De Socio GV, editor. PLOS ONE. 2017 May 31;12(5):e0178434.

19. Mehta JM, Haynes K, Wileyto EP, Gerber JS, Timko DR, Morgan SC, et al. Comparison of Prior Authorization and Prospective Audit with Feedback for Antimicrobial Stewardship. Infect Control Hosp Epidemiol. 2014 Sep 1;35(9):1092–9.

20. GolAli E, Sistanizad M, Salamzadeh J, Haghighi M, Solooki M. Antibiotic Prescribing Trends Before and After Implementation of an Audit and Feedback Program in Internal ward of a Tertiary Hospital in Tehran. Iran J Pharm Res [Internet]. 2019 Dec [cited 2023 Apr 5];18(4). Available from: https://doi.org/10.22037/ijpr.2019.1100833

21. Le Saux NMA, Bowes J, Viel-Thériault I, Thampi N, Blackburn J, Buba M, et al. Combined influence of practice guidelines and prospective audit and feedback stewardship on antimicrobial treatment of community-acquired pneumonia and empyema in children: 2012 to 2016. Paediatr Child Health. 2021 Jun 11;26(4):234–41.

22. Pett R. Audit and Feedback: A Quality Improvement Study to Improve Antimicrobial Stewardship. Fed Pract [Internet]. 2021 Jun 11 [cited 2023 Apr 5];(38 (6)). Available from: https://www.mdedge.com/fedprac/article/241305/mixed-topics/audit-and-feedback-quality-improvement-study-improve

23. McMullan BJ, Mahony M, Java L, Mostaghim M, Plaister M, Wu C, et al. Improving intravenous-to-oral antibiotic switch in children: a team-based audit and implementation approach. BMJ Open Qual. 2021 Mar;10(1):e001120.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.