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Review Article

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Role of Clinical Pharmacists in Reducing Antimicrobial Resistance: Systematic Review

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Abstract

Background: *Antimicrobial resistance is a global health challenge, and the world is more vulnerable to the adverse health impacts of antimicrobial resistance. Healthcare workers, including pharmacists, can play a key role in reducing antimicrobial resistance. There is little study done on the role of clinical pharmacy in reducing antimicrobial resistance, particularly in Ethiopia.*

Objective: *The aim of this review is to investigate the role of clinical pharmacists in reducing antimicrobial resistance.*

Method: *The databases MEDLINE, EMBASE, PUBMED, and Google Scholar were searched for articles published between 1999 and 2019 that involved studies on the role of clinical pharmacists and the expanded services of clinical pharmacists in the healthcare system and their contributions to antimicrobial use. PRISMA-2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) was used to conduct this review.*

Results: *Studies from different countries have demonstrated that the roles of clinical pharmacists in health care teams result in overall improved clinical and economic outcomes.*

Conclusions: *This review highlights that integration of clinical pharmacist services into healthcare systems will assist in reducing the growth of catastrophic antimicrobial resistance.*

Keywords: Antibiotics, Antimicrobial Resistance, Antimicrobial Stewardship Program, Clinical Pharmacists.

Abbreviations

CP: Clinical Pharmacist
AMR: Antimicrobial Resistance
WHO: World Health Organization
IPA: International Pharmaceutical Abstracts

1. Introduction

Antimicrobial Resistance (AMR) is defined as the resistance of bacterial, viral, parasitic, and fungal microorganisms to antimicrobial medicines that were previously effective for the treatment of infectious diseases. It occurs when bacteria, viruses, and other microorganisms change in ways that cause existing medications (e.g. antibiotics for bacterial infections and antivirals for viral infections) to be ineffective [1]. Infections caused by antibiotic-resistant microorganisms are associated with high morbidity, mortality, and healthcare costs; AMR annually causes 23,000 deaths in America, 25,000 deaths in the European Union, and 700,000 deaths worldwide. By 2050, it is predicted that there will be 10 million deaths annually and US$100 trillion in global economic loss caused by drug-resistant bacterial infections if AMR continues to rise at the same pace as in the last decades. Overprescribing and inappropriate prescribing of antibiotics are the principal and modifiable drivers of AMR [2].

Antimicrobial resistance is a serious global health challenge that impacts all countries and all people, regardless of their wealth or status. It is predicted that by 2050, there will be more than ten million deaths per year attributed to AMR. Further, it is predicted that the greatest number of these deaths will be in developing countries. Therefore, there is an urgent need to act to minimize the emergence of antimicrobial resistant bacteria in developing countries. The management of the development and spread of AMR requires a multifaceted approach, including the participation of all healthcare workers. According to the first objective of the

World Health Organization (WHO) global action plan on AMR, avoiding overuse and misuse of antibiotics requires healthcare professionals' awareness and understanding of AMR with effective communication, education, and training. In this context, a clinical pharmacist is a key member of the antimicrobial multidisciplinary team involved in patients' pharmacotherapy monitoring. Pharmacists are important members of the healthcare team and they play a major role in medicine use and the provision of advice regarding appropriate medicine use. Education and training of pharmacists has the potential to influence the behavior of healthcare team members and consumers as part of a multidimensional strategy for changing practice and ensuring the quality use of antibiotics [3]. Representative data on the extent of the problem in low and middle-income countries is relatively scarce, but high levels of resistance are increasingly being reported worldwide. Antibiotic stewardship, that is, interventions designed to optimize the use of antibiotics, is therefore one of the key actions of the World Health Organization (WHO) Global Action Plan to contain antibiotic resistance [4]. Although the role of multidisciplinary has been done in different countries to reduce AMR so far, there is no evidence that shows the role of clinical pharmacists alone in combating AMR. Therefore, the aim of this review is to investigate the role of clinical pharmacists in reducing antimicrobial resistance in hospital and community settings.

2.Methodology

2.1. Literature Search Strategy

A literature search was conducted to identify articles published between 1999 and 2019 that involved studies on antimicrobial use or AMR involving clinical pharmacists in hospital and community settings using databases such as MEDLINE, EMBASE, PUBMED, and Google Scholar. The following 'Medical Subject Headings' (MeSH) terms were used to search articles: (Antimicrobial agents or antibiotics) OR (Drug Resistance, Bacterial or Antimicrobial resistance) AND (clinical pharmacy or pharmacies) OR (community pharmacy services) OR (professional role/ or pharmacy service, hospital/or pharmacy/or pharmacists/or pharmacy practice.) OR (clinical pharmacy) AND (community pharmacist OR clinical pharmacist OR pharmaceutical care) AND (antimicrobial resistance or antibiotic cost).

Google Scholar was also used to search for articles with the appropriate keywords. The following search terms: Antibiotic stewardship, antimicrobial prescribing, clinical pharmacy, antibiotic consumption, physician's perception, clinical pharmacy, antimicrobial utilization, infectious disease; pharmacist intervention, antimicrobial stewardship, guideline adherence, pharmacist, urgent care, antibiotic, antimicrobials, intravenous, therapy-switch, pharmacist, clinical pharmacy, medication error, internal ward, cost, pharmacists, outcomes, interventions, multidisciplinary, hospital, antibiotic optimization, and antibiotic control programmers. The search words were used in different combinations. Cross-references of articles identified using these databases were also searched.

2.2. Eligibility Criteria

2.2.1. The Inclusion Criteria Were as Follows:

- Papers reporting descriptive accounts and papers reporting primary research involving an AMDT with pharmacy involvement
- Full-text papers published in peer-reviewed journals
- English-language full papers
- Papers involving interventions targeting hospital settings

2.2.2. The Exclusion Criteria Are as Follows

- Papers that were not available in full-text were discarded.
- Papers where there was either no multidisciplinary team or where the pharmacist had no role in the intervention were excluded.

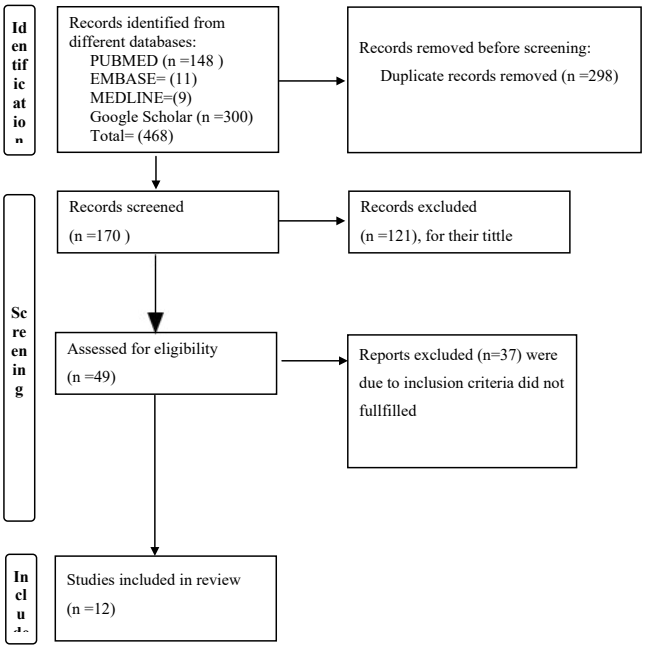

Figure 1: Flow chart of the systematic research and study selection process

3. Results

3.1. Searched Results

A total of 468 articles were obtained on initial searching from MEDLINE, EMBASE, PUBMED, and Google Scholar. A total of 298 articles were removed due to duplications. Finally, a total of 121 articles were excluded by observing their titles and abstracts. Consequently, only 37 articles were subjected to a full-text review. Finally, 12 articles were selected to be included in our review (Fig. 1).

3.2. Characteristics of Studies Included in This Review

In our review the filtered articles were pre and post interventional studies and randomized clinical trials studies. Articles included in this study were conducted on role of clinical pharmacist in reducing antimicrobial resistance. The majority of the studies were pre and post interventional studies in ten of the articles whereas RCTs in the two articles (Table 1) [5-16].

3.3. Rate of Reduction of Antimicrobial Resistance

Significantly less inappropriate doses for indication compared to the pre-intervention group (10.6% vs. 23.9%, p = 0.02), and less antibiotics prescribed for an inappropriate duration (15.8% vs. 32.4%, p < 0.01), more patients in the post intervention group had medications prescribed with appropriate dose, duration, and indication (51% vs. 66%, p = 0.04) [7]. Consumption of antimicrobials decreased from 48.9 % during pre-ASP to 36.9% in post-ASP (P = 0.001). The mean monthly antibiotic cost, during the pre-ASP was US$ 30,727.56, and US$ 9,623.73 in the last period of the study (P = 0.001) [Table 1] [10].

Author,Year [Reference]	Country	Setting	Objective	Study Design	Study Duration	Participants	Types of Intervention	Relevant Outcome	Outcome Measure	Total sample Size
N. Elkassas et al, 2018[5]	Egypt	General Hospital	To evaluate the acceptance of the role of the pharmacist in implementing antibiotic stewardship	Pre-post study	July,2014-Dec, 2015	Patients	CP involved in advising physicians about proper selection of antibiotics	Acceptance post intervention, (p<0.001) DRPs is reduced, compliance to clinical pharmacist by physician increased	Defined daily dose (DDD) per 1000 patient-days	805
Niaz Al-Somai.et al 2014 (6)	Saudi Arabia	Tertiary hospital	to measure the			Niaz Al-Somai.et al 2014 (6)	Saudi Arabia	Tertiary hospital	to measure the	357
Kiresten E. et al.2016 [7]	USA	Teaching hospital	To assess the impact of pharmacist intervention on appropriateness of antimicrobial prescribing on a geriatric psychiatric unit	Pre and post study	August 2014 - January 2015	Patients	CP reviewed patient chart and evaluated appropriateness of antimicrobial prescribing on geriatric psychiatric unit	Significantly less inappropriate doses for indication compared to the pre-intervention group (**10.6% *vs.* 23.9%**, *p* = 0.02), and less antibiotics prescribed for an inappropriate duration (15.8% *vs.* 32.4%, *p* < 0.01), more patients in the post intervention group had medications prescribed with appropriate dose, duration, and indication (51% *vs.* 66%, *p* = 0.04)	Percentage	133
N. Lauren, et al. 2019 [8]	USA	Hospital	To evaluate the impact of a pharmacist-led ASP in the urgent care setting	Pre-post study	2014 - 2016	Patients	N. Lauren, et al. 2019 [8]	Antimicrobial prescribing for all patients including all diagnoses was significantly improved during	pre- and post ASP compared by percentage	300

								the post-ASP period compared with the pre-ASP period (**53.3% and 41.3%,** respectively; $p = 0.037$)		
Hai-Xia Zhang. et al 2014 (9)	China	Tertiary hospital	To evaluate the impact and cost-benefit value of	pre and post study	January 1, 2011 to June 30, 2012	Patients	CP intervened real-time monitoring of medical records and controlling of the prescriptions of prophylactic	Prolonged duration of prophylaxis decreased from 7.58 days to 2.91 days ($p<0.001$). Mean antibiotic cost decrease from $338.59 to $98.95 (p, 0.001).] and	Cost benefit analaysis	370
								significant increase was observed in the rate of correct choice of antibiotics ($p< 0.001$) after the intervention		
Lucas M. et al. 2012 [10]	Brazil	Hospital	To assess the impact of an intervention-prospective audit with feedback to prescriber, with and without the presence of a pharmacist in ASP team	Pre-post study	January 2003 to December 2008	Patients	follow all patient-cases prospectively, recording the clinical data associated with the antimicrobial agent and the patient illness	Consumption of antimicrobials decreased from 48.9 % during pre-ASP to 36.9% in post-ASP ($P = 0.001$). The mean monthly antibiotic cost, during the pre-ASP was US$ 30,727.56, and US$ 9,623.73 in the last period of the study ($P = 0.001$)	mean monthly consumption in DDD/100 patient-days	250
Box MJ. et al 2015 (11)	California	Health care center	To assess impact of Pharmacists on ASP Teams in a Community Setting	Pre and post study	2011 - 2014	Patients	CP has a role in educational interventions and pharmacist led antimicrobial therapy duration of iv treatment	Improved the mean time to targeted antibiotic therapy (61.1 vs. 35.4 hrs; $p = 0.001$), reduced median time to positive culture from 3 days to 2 days ($p=0.0001$),	Mean, median and percentage	212
								Adherence to the antibiotic treatment was 48.4% in the CG and 67.2% in the IG, $p = 0.033$)		
Dunn K, et al. 201 1[12]	Ireland	university hospital	To assess the impact of the introduction of antimicrobial sub-committee-led, pharmacist delivered guidelines and	Pre-post study	December 2006 to June 2007	Patients	Application of stickers, guidelines to the drug chart, and providing consultation service to physician during	Significant reduction in the duration of IV antimicrobial treatment Improvement in the timeliness of IV to PO switch	Percentage and proportion	753

			criteria for switching from IV to PO antimicrobials				IV to PO switch by PC			
Angoulvant F et al. 2013[13]	France	tertiary pediatric hospital,	To evaluate therapeutic education delivered in a pediatric emergency care and attitudes about judicious	randomized controlled trial	February 2, 2009 to September 26, 2011	Patients	Therapeutic education on antibiotic was delivered by CP in the pediatric emergency department	parents satisfied with the information on antibiotics received was significantly higher (96.9% versus 83%, *P*=0.002)	percentage of parents satisfied	300
			antibiotic use							
Gross et al. 2001 [14]	USA	Tertiarycy Hospital	To improve the quality of patient care by ensuring the effectiveness of treatment regimens	Pre-post study	November 1993	Patients	Management of Antimicrobial recommendation	Better antimicrobial recommendations, cost effectiveness	Appropriateness use, cure and failure of the first regimen	180
H. Khalili et al. 2013 [15]	Iran	university Hospital	To evaluate the effect of clinical pharmacy services on medication costs	Pre and post study	September 2010 to September 2011	Patients	CP intervention involved with adding, discontinuation, and changing the frequency, duration or dose of drugs and Management of drug interactions, therapeutic drug level monitoring, stability of drugs and preventing medication error	Direct medication cost per patient was decreased ($160,140.5±12,445.1 versus $141,621.8±10,540.8), Hospitalization duration of patients reduced (15.8±4.9 versus 17.3±5.6 days, P<0.001) and total number of ordered medication per patient was reduced by 9±4.7 and 6.6±3.1 (P<0.001), CP recommendation on stability of drugs and	Percentage. and mean±standard deviation (SD)	1996
								preventing medication error was accepted 100% by nurses and physicians		
Gums et al, 1999 [16]	USA	Hospital	To identify financial and outcome benefits of therapeutic intervention by a multidisciplinary antimicrobial treatment team	RCT	September 1994 to March 1996	Patients	Clinical pharmacist involved in recommendations concerning antibiotic therapy and monitoring, as necessary	Median length of stay was reduced from 9 to 5.7 days, (p=0.0001) Median patient services' charges were reduced by	Mean cost Mean time	252

			composed of Pharmacists, a clinical microbiologist, and an infectious disease specialist.					$4404/intervention, (p=0.008) and median hospital costs were reduced by $2642/intervention (p=0.016)		

Table1: Summary of included studies on role of clinical pharmacist in reducing antimicrobial resistance in, Ethiopia

4. Discussion

The results of our study revealed that pharmacists' roles have expanded to provide multifaceted services in patient care, resulting in improved health outcomes from clinical services and reduced health care costs. This is consistent with the findings made in Australia [17]. In this review, the majority of articles showed the roles of clinical pharmacists in reducing the cost of antimicrobials, decreasing consumption of antimicrobials, significant reduction in duration of antibiotic use, and achieving optimal clinical outcomes related to antimicrobial use, which is in line with a study done at Peradeniya University in Australia in 2013[18]. Medications prescribed with appropriate dose, duration, and indication were observed in this study, which is in line with a study done at Louisiana University in the USA [19].

5. Conclusion

The provision of qualified clinical pharmacist services in healthcare systems has the potential to have a significant impact on reducing antimicrobial resistance. Studies from different countries have demonstrated that implementation of a pharmacist-led urgent care ASP, therapeutic advice, IV to PO conversion recommendation as per criteria, appropriate antimicrobial selection, and reduction of hospital stay and consumption of antimicrobials when they are recognized as part of the health care team. Antimicrobial stewardship involving pharmacists should be established in hospitals to ensure rational antimicrobial use. Therefore, integration of clinical pharmacist services into healthcare systems will assist in reducing the growth of catastrophic AMR.

Strengths and Limitations

To our knowledge, there have been few reviews of the actual or potential role of pharmacists in combating the challenge of AMR. This systematic review includes the novelty of summarizing the role of clinical pharmacists in reducing antimicrobial resistance available in literature. A limitation of this review is the inclusion of studies in English only, which can cause information bias. Moreover, only MEDLINE, EMBASE, PUBMED, and Google Scholar databases were searched. The absence of other databases such as Scopus could have introduced selection bias. While the authors discussed the inclusion criteria and data being extracted, there is still the potential for confusion bias.

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