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REVIEW

Impact of Clinical Pharmacist-led Interventions in Turkey

Türkiye'de Klinik Eczacı Tarafından Yapılan Müdahalelerin Etkisi

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ABSTRACT

Detecting drug-related problems (DRPs) is important in pharmaceutical care in for better therapeutic outcomes. Clinical pharmacists-led comprehensive medication management plays a crucial role in the rational use of drugs by preventing, identifying, and resolving DRPs. In this review, we aimed to determine the effect of interventions on patient outcomes performed by clinical pharmacists in Turkey. A systematic literature search was performed on PubMed, Google Scholar, EMBASE, Cochrane Library, and Turkish databases (ULAKBIM, Dergipark). The main categories were "clinical pharmacist", "intervention", and "Turkey". Two reviewers reviewed each article independently. Two independent reviewers screened all records and extracted data; disagreements were resolved through a consensus. Randomized controlled studies, pre- to post-intervention comparison studies, and cross-sectional studies including pharmacist-led interventions were included in the review. This review included 15 articles evaluating clinical pharmacist interventions. Ten studies (66.7%) focused on DRPs and pharmacist interventions to these problems, while the remaining 5 (33.3%) studies focused on patient education and adherence issues. Studies were conducted in oncology (33.3%), geriatrics (20.0%), chest diseases (13.3%), psychiatry (6.7%), cardiology (6.7%), and infectious diseases (6.7%) clinics. When results of studies are reviewed, most of the interventions were made at the prescriber level followed by the drug level and patient level. Problems were solved in 54.2-93.2% of DRPs, and adherence, patient knowledge, or skills were improved in most of the studies. Most of the studies were carried out within the scope of a postgraduate or doctorate thesis and yet various positive outcomes such as the prevention of side effects, increased quality of life, and decreased duration of hospital stay were observed with high positive rates of interventions, which indicate that other healthcare workers are ready to collaborate with the clinical pharmacists in Turkey.

Key words: Clinical pharmacy, drug-related problems, pharmaceutical care, clinical pharmacist, Turkey

ÖZ

İlaçla ilgili problemlerin saptanması (İİP), farmasötik bakım kapsamında daha iyi tedavi sonuçlarının sağlanması açısından önemlidir. Klinik eczacı tarafından yapılan kapsamlı ilaç yönetimi, ilaçla ilgili problemleri önleyerek, tanımlayarak ve çözerek ilaçların rasyonel kullanımında önemli bir rol oynamaktadır. Bu derlemede, Türkiye'de klinik eczacı tarafından yapılan müdahalelerin hasta sonuçları üzerindeki etkisinin belirlenmesi amaçlanmıştır. PubMed, Google Akademik, EMBASE, Cochrane Kütüphanesi ve Türk veri tabanlarında (ULAKBIM, Dergipark) sistematik bir literatür taraması yapılmıştır. Ana kategoriler "klinik eczacı", "müdahale" ve "Türkiye" olarak belirlenmiştir. İki araştırmacı her makaleyi bağımsız olarak gözden geçirmiştir. İki bağımsız araştırmacı ise tüm kayıtları taramış ve verileri elde etmiş; anlaşmazlıklar fikir birliği ile çözülmüştür. Eczacılar tarafından yapılan müdahaleleri içeren randomize kontrollü çalışmalar, müdahale öncesi ve sonrası karşılaştırma çalışmaları ve kesitsel çalışmalar derlemeye dahil edilmiştir. Bu derlemeye, klinik eczacı müdahalelerini değerlendiren 15 makale dahil edilmiştir. On çalışma (%66,7) ilaçla ilgili problemler ve bu problemlere eczacı müdahalelerine odaklanırken, geri kalan 5 (%33,3) çalışma hasta eğitimi ve uyunç konularına odaklanmıştır. Çalışmalar, onkoloji (%33,3), geriatri (%20,0), göğüs hastalıkları (%13,3), psikiyatri (%6,7), kardiyoloji (%6,7) ve enfeksiyon hastalıkları (%6,7) kliniklerinde yapılmıştır. Çalışmaların sonuçları incelendiğinde, müdahalelerin çoğu hekim düzeyinde, daha sonrası ise ilaç düzeyi ve hasta düzeyinde yapılmıştır. İİP'lerin %54,2-93,2'sinde problem çözülmüştür ve çalışmaların çoğunda uyunç, hasta bilgisi veya becerileri geliştirilmiştir. Çalışmaların çoğunluğu yüksek lisans veya doktora tezi kapsamında yapılmıştır. Müdahalelerin yüksek kabul oranlarının yanı sıra, yan etkilerin önlenmesi, yaşam kalitesinde artış ve hastanede kalış süresinde azalma gibi çeşitli olumlu sonuçlar gözlenmiştir. Bu sonuçlar Türkiye'deki diğer sağlık çalışanlarının klinik eczacılarla iş birliği yapmaya hazır olduklarını göstermektedir.

Anahtar kelimeler: Klinik eczacılık, ilaçla ilgili problemler, farmasötik bakım, klinik eczacı, Türkiye

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INTRODUCTION

A drug-related problem (DRP) is defined as "an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes".[1,2] Detecting DRPs is important in pharmaceutical care, as DRPs are related to treatment outcomes. To identify and resolve DRPs in terms of rational drug use, clinical pharmacist-led comprehensive medication management plays a crucial role.[2,3]

Clinical pharmacists beyond the many other duties primarily provide pharmaceutical care to improve treatment adherence and to decrease DRPs.[4-6] The quality of care may be improved by pharmaceutical care services in many diseases like hypertension,[7] asthma,[8] hyperlipidemia,[9] and diabetes.[10] The first step in pharmaceutical care services is identifying patients' pharmaceutical care needs and the second step is developing an individualized pharmaceutical care plan, with respect to the patient's knowledge, attitudes, and motivation. The third step is evaluating the outcomes of the pharmaceutical care plan. Finally, the fourth and fifth steps consist of implementing the care plan and continuous monitoring, respectively.[11]

Clinical pharmacy services, including pharmaceutical care, has developed in the USA in the 1960s. It has changed over time in terms of concept and the variety of practices.[12] It has been linked to proper prescribing, preventing or reducing DRPs, adverse drug events, quality of life (QoL), medication errors, and cost charged during the treatment.[13-18] According to the International Pharmaceutical Federation consensus report in 2009, clinical pharmacy services given should be global, which was established in many developed countries[19] including Turkey.[20]

Clinical pharmacy service is a relatively new and developing concept in Turkey.[21] The first discussions started in 1986.[22] It has been performing since 1991 and was started at Marmara University, which opened the first postgraduate education program. In 1994, clinical pharmacy course was a part of undergraduate education at Hacettepe University. In 1997, Ankara University established the interdisciplinary clinical pharmacy postgraduate education program. In 1998, to promote clinical pharmacy in Turkey, "The Society of Clinical Pharmacy, KED" was established. Since 2003, many continuing education programs were organized by both KED and the "Turkish Pharmacists' Association Academy of Pharmacy" on clinical pharmacy and pharmaceutical care.[21] In Turkey, the first Department of Clinical Pharmacy was established at Hacettepe University in 2013, and thereafter at Marmara University and Inonu University.[23] Although clinical pharmacy was established as a subdivision at Marmara University many years ago (1995) and allowed to open a department throughout Turkey in 2013, it still operates as a subdivision under the pharmacology department in some universities due to a lack of academic staff. Furthermore, in 2014, with the approval of the Grand national assembly of Turkey, clinical pharmacy became a legal specialty supported by "Law on pharmacies and pharmacy". According to this law, pharmacists may take a special exam once a year and based on the scores of this exam, and a limited number of them may start the 3-year postgraduate clinical pharmacy specialty education in selected universities.[24]

As mentioned above, as a member of the multidisciplinary and interdisciplinary team, the clinical pharmacist has a significant role in improving the treatment, patient outcomes, and QoL. The positive impact of clinical pharmacist-led interventions on patient outcomes in terms of reduced hospital visits and mortality was reported in other countries.[25,26] Another impact of clinical pharmacists is on the pharmacoeconomic parameters. Studies show that there is proven evidence on the economic benefits of clinical pharmacy services via reducing the total healthcare costs in various health departments.[13,14]

It is important to show nation-wide results from a developing science to emphasize weak and strong sides and guide complete education. This review aimed to present the impact of interventions performed by clinical pharmacists in Turkey on patient outcomes and shows an inside view of what has been done since the implementation of the clinical pharmacy program in Turkey, and to lead further comprehensive studies.

A systematic literature search (up February 20, 2020) was performed according to PICOS formatting on PubMed, Google Scholar, EMBASE, Cochrane Library, Turkish databases (ULAKBIM, Dergipark) with the headings "clinical pharmacist", "intervention", and "Turkey" with "AND" and "OR" operators. Two reviewers (EK and BKC) reviewed each article independently. The search strategy of PubMed was as per the following: ["pharmacists" (MeSH Terms) OR "pharmacists"(All Fields)] OR ["clinical"(All Fields) AND "pharmacist"(All Fields)] OR "clinical pharmacist" (All Fields) AND ["Turkey"(MeSH Terms) OR "Turkey"(All Fields)].

The general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements were used. Two independent researchers screened records, further extracted data, and disagreements were resolved through a consensus. Extracted data and quality assessment variables were presented in tables with a narrative description. Randomized controlled studies, pre- to post-intervention comparison studies, and cross-sectional studies which included pharmacist-led interventions were included. Even though abstracts, letters, and case reports were also read and evaluated, articles with no full-text, conference reports, reviews, editorials, letters, or case reports were excluded. Articles referring to countries other than Turkey were excluded. First author's name, publication year, study design, the type of clinical pharmacist-led interventions, patient age, patient outcomes, and the acceptance rate of interventions were evaluated. The first author (EK) extracted the data, and another review author (BKC) did the double-checking. If there was any conflict, another author (MS or KD) made the final decision.

To prevent bias in individual studies, every researcher extracted data other than their study. Data extraction was undertaken by one reviewer using a tailored data extraction

framework, developed to explicit data extraction elements related directly to the review question for the qualitative studies. All of the extractions were checked by a second reviewer. No additional analyses were made to combine the data.

This review included 15 articles out of 94 publications evaluating clinical pharmacist interventions in Turkey (Figure 1). The oldest article included in this review was published in 2007 and the latest was published in 2020. The distribution of publishing years of the articles is given in Graphic 1. The majority of the articles were published in Science Citation Index-Expanded indexed journals that were ranked in the third quartile and fourth quartile. The characteristics of the journals in which the articles were published are listed in Table 1. The study design of two (13.3%) of the 13 articles included were retrospective, while the remaining 13 (86.7%) were prospective. Ten studies (86.7%) focused on DRPs and pharmacist interventions to these problems, while the remaining five (33.3%) studies focused on patient education and adherence issues. Different versions of the Pharmaceutical Care Network Europe (PCNE) DRPs classification system was used in seven (46.7%) of the studies. Different tools, such as Beers' criteria, screening tool of older persons' potentially inappropriate prescriptions criteria, screening tool to alert doctors to the right treatment criteria and National Cancer Institute common toxicology criteria for adverse effects version 4, were used in other studies.

Studies were conducted in oncology (n=5, 33.3%), geriatrics (n=3, 20.0%), chest disease (n=2, 13.3%), psychiatry (n=1, 6.7%), cardiology (n=1, 6.7%), infectious diseases (n=1, 6.7%), and in clinical and community pharmacy (n=2, 13.3%). The studies were conducted in the inpatient (n=6, 40.0%), outpatient (n=7, 46.7%), and community pharmacy (n=2, 13.3%) settings. The characteristics of the studies, patients, and interventions are listed as Table 2.

The duration of the studies was between 3 to 11 months, the number of patients in the studies were between 25 and 186, and the average age of the patients included in the studies was between 33 and 80 years.

When the study outcomes were reviewed, most of the interventions were made at the prescriber level, followed by drug level, and patient level. Problems were solved in a median of 86% (54.2-93.2%) of DRPs, and adherence, patient knowledge, or skills were improved in these studies (Table 2).

Table 1. The characteristics of the journals in which articles were published

Journal name	First author and year	Indexing	Impact factor	Quartiles
International Journal of Clinical Pharmacy (formerly Pharmacy World & Science)	Umar et al.[27] (2020)	SCI-expanded	1.941 (5-years)	Q4
Journal of Oncology Pharmacy Practice	Kucuk et al.[28] (2019)	SCI-expanded	1.826 (2018)	Q3
Clinical Interventions in Aging	Ertuna et al.[29] (2019)	SCI-expanded	3.195 (5-years)	Q3
International Clinical Psychopharmacology	Yalcin et al.[30] (2019)	SCI-expanded	2.169 (5-years)	Q4
Journal of Research in Pharmacy (formerly Marmara Pharmaceutical Journal)	Izzettin et al.[31] (2019)	Emerging-SCI	0.14 (2018)	-
Turkish Journal of Medical Sciences	Kara et al.[32] (2019)	SCI-expanded	0.698 (5-years)	Q4
Journal of Oncology Pharmacy Practice	Paksoy et al.[33] (2018)	SCI-expanded	1.826 (2018)	Q3
UHOD-Uluslararasi Hematoloji-Onkoloji Dergisi	Tecen-Yucel et al.[34] (2018)	SCI-expanded	1.667 (5-years)	Q4
Marmara Pharmaceutical Journal	Izzettin et al.[35] (2017)	Emerging-SCI	0.14 (2018)	-
European Journal of Hospital Pharmacy-Science and Practice	Tezcan et al.[36] (2016)	SCI-expanded	0.661 (5-years)	Q4
Respiratory Medicine	Apikoglu-Rabus et al.[37] S. (2016)	SCI-expanded	3.702 (5-years)	Q2
Pharmazie	Selcuk et al.[38] (2015)	SCI-expanded	1.004 (5-years)	Q4
European Journal of Hospital Pharmacy-Science and Practice	Sancar et al.[39] (2015)	SCI-expanded	0.661 (5-years)	Q4
Pharmacy World & Science	Turnacilar et al.[40] (2009)	SCI-expanded	1.429 (5-years)	Q3
American Journal of Health-System Pharmacy	Clark et al.[41] (2007)	SCI-expanded	2.427 (5-years)	Q3

SCI: Science citation index

Table 2. The characteristics of the studies, patients, and interventions

First author and design	Title	Population and monitoring time	Age of population	Clinical pharmacist interventions	Major outcomes
Umar et al.[27] (2020) Prospective study	Significance of a clinical pharmacist-led comprehensive medication management program for hospitalized oncology patients	137 oncology patients 5 months	58±14.60	Identification and classification of DRPs were performed by using the PCNE classification V6.2.	A total of 481 DRPs were identified in 114 patients. The majority (69%, n=332) of interventions were made at the prescriber level, while 29.3% (n=141) interventions were made at the drug level, most of which included beginning a new medication (11.4%, n=55) or stopping a medication (9.6%, n=46). The majority (n=437; 90.9%) of the problems were solved
Kucuk et al.[28] (2019) Descriptive, prospective study	Drug-related problems with targeted/ immunotherapies at an oncology outpatient clinic	54 oncology patients in the outpatient setting 3 months	57±11.98	DRPs were identified by a clinical pharmacist in patients receiving targeted chemotherapy and/or immunotherapy. PCNE classification v.7 was used.	During the study period, a total of 105 DRPs (1.94 per patient, 0.38 per consultation) were identified. A total of 149 planned interventions were recorded by the clinical pharmacist of which 8 (5%) were at the prescriber level, 23 (15%) were at drug level, 92 (62%) were at patient level, and 14 (9%) were other interventions or activities. As a result, 68 (65%) out of 105 DRPs were resolved
Ertuna et al.[29] (2019) Retrospective study	Evaluation of pharmacist interventions and commonly used medications in the geriatric ward of a teaching hospital in Turkey: A retrospective study	91 geriatric patients Weekly order review for about 8 months	80±0.46	Problems were classified according to the PCNE classification system v8.02. PIM use was determined by using Beers and STOPP/ START criteria	A total of 329 possible DRPs were detected in 156 orders, of which 282 (85.71%) interventions were proposed to the prescribers. On 47 (14.28%) occasions, the prescriber was only informed, or the intervention was discussed with the prescriber. The acceptance rate of pharmacist interventions was 85.41% (n=281) and 38 (11.55%) of the proposed interventions were rejected by the physician
Yalcin et al.[30] (2019) Prospective study	Compliance in schizophrenic spectrum disorders: Role of clinical pharmacist	40 patients with schizophrenic spectrum disorder 10 months, during hospitalization and 4-6 weeks following discharge	33±10.99	PANSS, ROMI, UKU, SAS, BARS were used	Twenty-three (57.5%) patients showed poor compliance at the first interview, while only 7 (17.5%) patients recorded with poor compliance at the second interview after drug education (average total MARS scores of the first and second interviews were, respectively, 6.6 (2.23) and 8.6 (1.29); ($p<0.001$). According to ROMI, the number of patients who wanted to use medicaion was detected 35 (87.5%) during the first intervention and 39 (97.5%) during the second intervention

Table 2. Continued

First author and design	Title	Population and monitoring time	Age of population	Clinical pharmacist interventions	Major outcomes
Izzettin et al.[31] (2019) Prospective, cross-sectional randomized study	The role of the clinical pharmacist in patient education and monitoring of patients under warfarin treatment	25 patients diagnosed with venous thromboembolism or prosthetic valve replacement in a cardiology clinic 3 months	53±2.18	Pre- and post-test to evaluate the level of knowledge of the patients on oral anticoagulant. The quality of life was measured by SF-36 and the DASS tests were applied	After three months of the study, the SF-36 Physical Component Score and SF-36 mental component score were increased and results were statistically significant. The number of correct answers of the patients in the pre-test was increased and results were statistically significant after three months of the study ($p < 0.001$). Total DASS scores, DASS "limitation" scores, DASS "burden" scores, and DASS "positive effect" scores were improved ($p<0.05$).
Kara et al.[32] (2019) Prospective, cross-sectional study	Polypharmacy and drug-related problems among people living with HIV/AIDS: A single-center experience	186 PLWHA in an infectious disease outpatient clinic 11 months	40±13.1	Followed by a pharmacist interview with PLWHA, the official recommendation was offered to the attending physician and the participants, which encompassed treatment, drug interactions, and side effects. PCNE classification v7.0 was used	Fifty-eight DRPs were found in 45 patients. Twenty-nine (50%) of the interventions were made to the physicians alone, 25 (43%) to the patients alone, and 4 were made to both the physicians and the patients. Twenty-nine (50%) interventions involved comorbidities or co-medications and 19 (32.8%) of these involved anti-retroviral drugs. In this study, 93.2% of the interventions were accepted by the physicians
Paksoy et al.[33] (2018) Prospective study	Evaluation of potentially inappropriate medication utilization in elderly patients with cancer at outpatient oncology unit	114 elderly patients oncology outpatient clinic 4 months	71.78±5.50	Medication review to determine PIMs and POMs made by using STOPP/START criteria	In 94.73% of the patients, polypharmacy was detected. STOPP criteria were applied to a total of 114 patients and 20 PIM uses in 18 patients were found and interventions were accepted by the clinicians. According to the START criteria, a total of 221 medication omissions in 112 patients were found and interventions were accepted by the clinicians. The number of non-cancer medications and the total number of medications was statistically high according to the presence of STOPP criteria ($p<0.001$)
Tecen-Yucel et al.[34] (2018) Descriptive, cross-sectional, prospective study	Clinical pharmacy practices in oncology patients treated with tyrosine kinase inhibitors	55 medical oncology outpatient clinic patients 3 months	60 (range 28-79)	TKI-related adverse effects were monitored and evaluated by using the NCI-CTCAE version 4.	A total of 92 interactions were detected, and 54 (58.7%) were evaluated as clinically significant and required intervention. A total of 32 recommendations for the management of adverse effects were provided by a clinical pharmacist and 29 (90.6%) were accepted by the consultant physicians. Clinically significant improvements in patients were observed in criteria related to dry skin, diarrhea, fatigue, infection, hematuria, acute kidney injury, vomiting, salivary duct inflammation, and alanine aminotransferase levels between the first and second visits

Table 2. Continued

First author and design	Title	Population and monitoring time	Age of population	Clinical pharmacist interventions	Major outcomes
Izzettin et al.[35] (2017) Prospective study	Influence of pharmacist recommendations for chemotherapy-related problems in diabetic cancer patients	50 diabetic patients with a new diagnosis of diverse types of cancers 8 months	61±8.99	The assessment of DRPs was based on PCNE classification V6.2.	In this study, 69.57% (n=80) of the DRPs were solved due to recommendations by the clinical pharmacist. After clinical pharmacist recommendations and provision of patient education, a significant decrease in the occurrence (first vs. second readings) and severity (mild vs. moderate) of adverse drug effects was observed as a mild urinary frequency (p=0.0001) and mild vomiting (p=0.0001)
Tezcan et al.[36] (2016) Prospective study	Role of clinical oncology pharmacist in the determination of pharmaceutical care needs in patients with colorectal cancer	36 colon cancer patients in the outpatient chemotherapy un 5 months, during three chemotherapy courses	58±12.86	The symptom-based quality of life questionnaires were administered before the first and after the third course of chemotherapy. Potential DRPs were recorded	DRPs decreased within the third course of chemotherapy compared with the first course after interventions. A total of 147 recommendations were given and of those, 52.4% (n=77) were non-pharmacological and 47.6% (n=70) were pharmacological. One hundred and forty-four (98%) recommendations were followed by patients. Of the recommendations followed, 91.7% (=132) were succeeded to solve the DRP, while 8.3% (n= 12) were failed to solve the problem.
Apikoglu-Rabus et al.[37] (2016) Prospective study	Drug-related problems and pharmacist interventions in a cohort of patients with asthma and chronic obstructive pulmonary disease	44 patients with asthma and 37 patients with chronic obstructive pulmonary disease 6 months	Asthma patients: 52.4±1.9 COPD patients: 65.9±10.5	DRPs were identified at the initial visit using the Turkish version of the PCNE Classification scheme for drug-related problems v6.2. In addition, MMAS was used	Only five patients with asthma (11.4%) and four patients with COPD (10.8%) were highly adherent with their medication regimen. Fifty-nine DRPs were identified for 44 patients with asthma, of which 93% were manifested and 7% were potential. A majority of these problems (98%) were identified by the pharmacist. A total of 134 causes were identified for 59 problems. Sixty were identified for 37 patients with COPD, with 88% of the problems manifested, while 12% were potential. A majority (95%) of these problems were identified by the pharmacist. A total of 128 causes were identified for 60 problems. A total of 84 interventions were provided for the patients with asthma, and 95 interventions were provided for the patients with COPD. Most of the interventions were made at the patient level (81% on asthma patients and 80% on COPD patients). Almost half of the problems were solved (54.2% on asthma patients and 63.3% on COPD patients)

Table 2. Continued

First author and design	Title	Population and monitoring time	Age of population	Clinical pharmacist interventions	Major outcomes
Selcuk et al.[38] (2015) Retrospective study	The potential role of clinical pharmacists in elderly patients during hospital admission	133 hospitalized elderly patients 4 months, weekly participation in the ward	77±8.12	Medication discrepancies were determined and divided between intended and unintended discrepancies. All DRPs were determined regarding home and hospital medications according to PCNE classification, v.6.2	The utilization of high alert medications was seen in 77.4% of the patients. The PIM was found in 19.5% of elderly patients. A total of 394 medication discrepancies were detected and classified as either intended or unintended discrepancies. The clinical pharmacist was presented a total of 396 recommendations to the physician on the ward and the physicians were accepted 85.6% of them
Sancar et al.[39] (2015) Prospective, pre- and post-intervention study	The effect of pharmacist-led education on inhaler use skills in hospitalized patients with chronic obstructive pulmonary disease	41 hospitalized patients with COPD 9 months, clinic visit was arranged for a month later from hospital discharge (2 days/week)	64±11.78	The clinical pharmacists used verbal instruction and printed and demonstration materials to educate patients on the correct methods for using each inhaler device according to the GOLD guideline	Patients' inhaler administration skills were found to be improved by pharmacist-led education ($p<0.05$). Statistically significant improvement in patient inhaler use skills were obtained for every scored item except removing the cap before starting to use inhalers following pharmacist-led education. The improvement in appropriate inhaler device usage techniques following pharmacist-led education was also determined when evaluating patients' attitudes toward the different types of inhalers. An increase in the rate of mouth rinsing after corticosteroid inhalation was observed in the following pharmacist-led training (38.2% vs 91.2%)
Turnacilar et al.[40] (2009) Prospective, longitudinal study	Improvement of diabetes indices of care by short pharmaceutical care (PC) program	43 patients with type 2 diabetics visiting community pharmacies 7 months retrospective	62±1.50	Retrospective data of past 3 months were collected using a standard self-administered questionnaire	Nine (20.9%) patients used to perform SMBG before PC; this number increased to 13 (30.2%) patients after PC ($p<0.05$). After PC, this number increased to 95.3% ($p < 0.001$). During the PC period, two out of twelve smoking patients quit smoking and reported being smoke-free until the end of the PC period. The barriers to adherence were identified and managed in the two patients
Clark et al.[41] (2007) Prospective, randomized, case-control study	Effect of pharmacist-led patient education on adherence to tuberculosis (TB) treatment	154 hospitalized, newly diagnosed tuberculosis TB patients 8 months, two months during inpatient clinics, and six months after discharge	Newly diagnosed TB patients: 38±14.0 Multi-drug resistant (MDR) TB patients: 43±2.50	In the first interview, patients' health beliefs and knowledge on their current drugs and doses were assessed through an interviewer-assisted questionnaire. The clinical pharmacist provided standard oral and written patient education to the patients in the education group shortly before the discharge	The effect of pharmacist-directed patient education in terms of improving visit was statistically significant ($p<0.05$). The number of patients who attended all the scheduled visits were higher in the education group than in the non-education group (53.6% vs. 29.3%, respectively). The beneficial effect of patient education on the positive isoniazid test result percentage was statistically significant ($p=0.001$). The drug-related issues were again similar for newly diagnosed TB and MDR-TB patients

PIM: Potentially inadequate medication, STOPP: Screening tool of older people's prescriptions, START: Screening tool to alert to right treatment, PANSS: Positive and negative syndrome scale, MARS: Medication adherence rating scale, ROMI: The rating of medication influences, UKU: Udvalg for Kliniske Undersogelser, SAS: Simpson-Angus, abnormal involuntary movement scale, BARS: Barnes Akathisia rating scale, SF-36: Short form 36, DASS: Depression anxiety stress scales, HIV: Human immunodeficiency virus, AIDS: Acquired immunodeficiency syndrome, PLWHA: People living with HIV/AIDS, POM: Potential prescribing omission, TKI: Tyrosine kinase inhibitors, NCI: National Cancer Institute, CTCAE: Common Terminology Criteria for Adverse Events, COPD: Chronic obstructive pulmonary disease, MMAS: Morisky medication adherence scale, GOLD: The Global Initiative for Chronic Obstructive Lung Disease

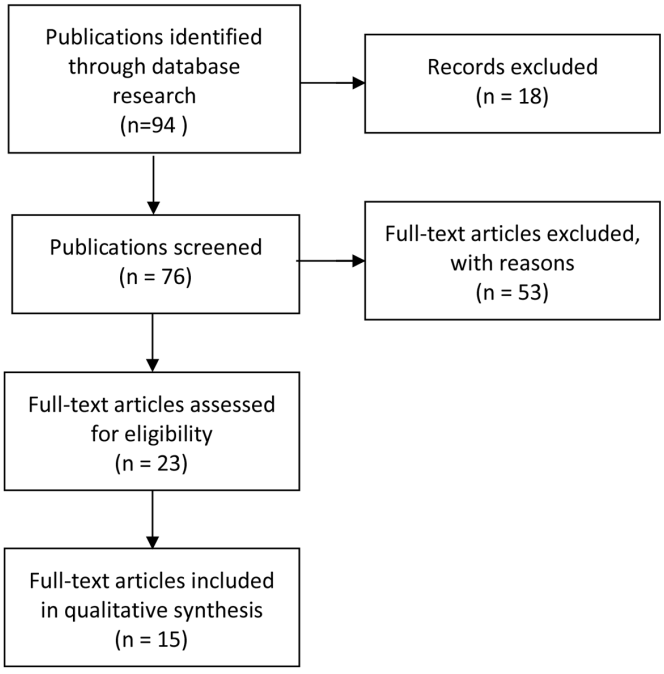
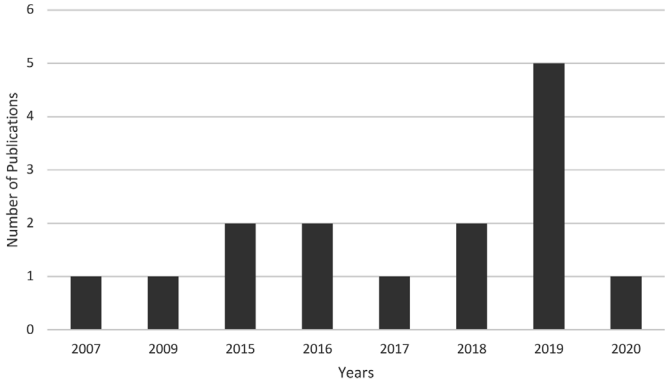


Figure 1. Article selection process



Graphic 1. Distribution of publishing years of the articles

DISCUSSION

According to our perspective, ours is the first study that reviewed the studies in the field of clinical pharmacy in Turkey. Clinical pharmacy services in Turkey still have not entered routine practices. It is thought that it will become a routine practice by 2023.[24] Most of the studies included in this review were carried out within the scope of a postgraduate thesis. Therefore, most of these studies focused on clinical pharmacy services that were offered for the first time to the clinicians or patients. Because clinical pharmacists are still not a routine member of the interdisciplinary team, these studies were unable to address all the identified pharmaceutical care needs, and for the same reason, the duration of studies was limited to few months.

The findings of decreased adverse drug effects, improved appropriate prescribing, shortened length of hospital stay (LoS), and reduced costs were reported in many other studies from outside of Turkey.[13,18,42] The outcomes of the interventions were beneficial in terms of visualizing clinical pharmacy activities and better results in patients. Positive outcomes were observed, such as reduction or prevention of side effects, improvement in QoL, and reduction in LoS in the hospital with the high acceptance rates of interventions by the physicians, which indicate that despite the obstacles that faced in clinical pharmacy services, other healthcare professionals are ready to collaborate with the clinical pharmacists in Turkey.

In China, it was determined that appropriate prescribing and patient knowledge about medications was enhanced with the implementation of clinical pharmacy practices both in inpatient and outpatient settings.[43] Rotta et al.[44] overviewed 49 systematic reviews between 2000-2010 and found that clinical pharmacy practices were focused on certain chronic diseases like blood pressure and glucose control. Due to the variability of methods, interventions about medication adherence and prescription appropriateness caused inconclusive results.

Pehlivanli et al.[45] reviewed 46 articles published between 2006 and 2016 on the role of the clinical pharmacist. They found that the studies were mostly related to cardiovascular diseases (13%), adverse drug events (11%), and infectious diseases (9%). The evaluated studies were generally prospective, observational, or interventional studies.[45] In Turkey, there were also studies conducted within the scope of clinical pharmacy but without pharmacist intervention. Adverse effects and compliance with antidepressants in patients with major depression were evaluated by Sancar et al.[46] Most commonly in 56 patients, side effects such as dizziness, dry mouth, increased sleep were observed, and 73.2% of the patients were found to have low compliance with the treatment. In addition to the routine service they receive from the outpatient clinic, it is concluded that educating and monitoring the side effects and compliance by the pharmacists will contribute to preventing possible DRPs.[46] In another study, the appropriateness of drug treatment was evaluated, and requirements of pharmaceutical care were identified in geriatric patients. A low level of knowledge about drug usage was detected in patients, and they were not informed about the proper drug use.[47] Okuyan et al.[48] aimed to evaluate the knowledge and attitudes of type 2 diabetic patients regarding the use of a disposable insulin pen. As a result of this study, missing or improper usage of the disposable insulin pen was observed in hospitalized patients.[48] The patient risk score was used by Aras et al.[49] to evaluate the risk of febrile neutropenia (FN) and to assess granulocyte colony-stimulating factors use, and its side effects in an outpatient clinic. They found that inadequate or unnecessary treatments should be evaluated for the risk of FN in each chemotherapy cycle and that a routine risk assessment can also be implemented.[49] Abunahlah et al.[50] conducted a study in internal medicine wards to identify DRPs in a teaching and research hospital in Istanbul, Turkey. In this study, 163 DRPs were determined by using the PCNE classification V 7.0 in 100 patients that used a total of 808 drugs. According to their results, age, LoS in hospital, number of drugs, renal impairment, and inflammation correlated with the causes of DRPs, and age, number of drugs, LoS in hospital, renal dysfunction, liver failure, diagnosis, and comorbidities correlated with the number of DRPs.[50]

Another concern is appropriate measures for the effectiveness of pharmacists' services. Hospitalization, mortality, or outpatient visits should be used for the evaluation of effectiveness endpoints; however, an extended duration of follow-up periods is needed to demonstrate a potential input for these endpoints. Thus, intermediate or surrogate indicators may be used to evaluate the short-term effects of interventions. Short-term evaluation methods of the included studies were also explained in this review.

The American College of Clinical Pharmacy (ACCP) defined that clinical pharmacists are a primary source of scientifically valid information and advice regarding the safe, appropriate, cost effective use of medications, and optimizing medication therapy with the background of pharmaceutical care. They routinely provide updated knowledge that contributes to improved health and QoL to patients and healthcare professionals.[51] According to the definition by ACCP, clinical pharmacists in Turkey are also contributing to many research projects in the field of clinical pharmacy and in various other health-related fields. They provide immense knowledge to other healthcare professionals. Since these publications were outside the scope of this study, they were not discussed.

The main limitations of the studies reviewed in this were study setting (one hospital) and the study size (small groups).[28,29,32,34] Other limitations were retrospective evaluations of pharmacist interventions[29,38] and the absence of a control group for comparisons.[28] Additional controlled and prospective studies are also in progress for publication due to ongoing thesis or projects in Turkey. A significant expansion in the number of publications is expected due to the increase in the number of both graduates and special program graduates who were trained in the field of clinical pharmacy in the recent years.

The limitations of this review were that even though a literature search was conducted on different databases, there might have been omitted or overlooked studies. PRISMA checklist items could not be fully followed because the studies included in this review were not homogeneous, and the available studies were few. Future studies are needed to assess the impact of clinical pharmacist interventions on health expenditure in Turkey by using cost-effectiveness or cost-benefit analysis methods.

CONCLUSION

In conclusion, there is a growing practice of clinical pharmacy in Turkey; however, a clear definition of clinical pharmacy services, implementation to the routine healthcare team, and standardized methods that assess the impact of these services on patient health-related outcomes are still needed. It is shown that even with the institutional effort, clinical pharmacy services may make a strong contribution to the Turkish healthcare system, but for providing a trustworthy and sustainable service, governmental and educational support should be developed.

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