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The Impact of Computerized Physician Order Entry (CPOE) Combined with Clinical Decision Support System (CDSS) On Preventing Adverse Drug Reactions In Renal Insufficiency: Systematic Review

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Abstract

Background: Renal impairment influences a wide range of interventions, and improper actions may lead to many life-threatening complications. The kidney is one of the most important organs for the metabolism of medications. Adverse drug reactions in renal dysfunctional patients are often overlooked when prescribing medications. Implementing innovative technologies such as Computerized Physician Order Entry (CPOE) and Clinical Decision Support System (CDSS) may alleviate these concerns. This study aims to clarify the impact of implementing CDSS and CPOE technology into the healthcare system environment and preventing ADR in patients suffering from renal insufficiency and diseases by systematically reviewing the literature.

Methods: Systematic review was conducted using proper article appraisal, study selection, and results synthesis.

Results: We identified 5 out of 168 articles and were included in this review, following appraisal and PRISMA workflow. 2 studies were RCT, 1 quasi-experimental, 1 retrospective, and 1 alternating time-series. 3 studies focused on nephrotoxic medication adjustment in renal impaired patients. 1 study explored the impact of the various CDSS level of sophistication on renal patients. 1 study shed light on the overdosing of ER physicians for renal impaired patients and the impact of implementing a CDSS for better patient's safety.

Conclusion: CPOE coupled with CDSS demonstrated an overall positive impact on the quality of care for patients suffering from renal impairment by detecting possible adverse drug reactions. Further, quality research is needed to truly evaluate the impact of CPOE and CDSS in the healthcare domain.

Keywords: Computerized Physician Order Entry (CPOE); Clinical Decision Support System (CDSS); Adverse Drug Reactions; Renal Insufficiency.

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1. Introduction

Renal impairment is one of the most important concerns to take into account in the medical field as it influences a wide range of interventions and leads to many complications; some are life-threatening. Renal diseases such as chronic kidney disease (CKD) affect almost 10% of the population worldwide and in 2017, 1·2 million people died from CKD globally. Furthermore, the mortality rate from CKD increased by 41.5% between 1990 and 2017 [1].

kidney is one of the major sites responsible for drug excretion and elimination, renal function impairment due to acute or chronic disease may lead to increased concentrations of drugs in the body and lead to drug accumulation, which in turn may lead to serious toxicity issues and harm [2]. These are especially important in the case of drugs that are primarily eliminated by the kidneys [3]. Concentration-sensitive medications such as seizure and antiepileptic drugs may lead to adverse drug reactions while also being nephrotoxic and require dose adjustments based on the renal function profile of each patient [4].

Hospital admissions due to adverse drug reactions (ADR) varies from 1.3% to 41.3%, with the average rate of 15.4% of all hospitalization [5]. Renal insufficiency is a well-established risk factor in ADRs and accounts for almost 3-10 times the incidence rate compared to healthy patients. [6]. Multiple studies summarized and gave examples of ADRs in patients suffering from renal insufficiency. Zand et al. (2010) highlighted that inappropriate Gabapentin dosing, an analgesic commonly used in patients with chronic kidney disease with low eGFR (<90 mL/min/1.73 m2), leads to adverse drug events (ADE) in up to 77.8% in some groups [9]. Likewise, Sharif-Askari, Fatemeh Saheb, et al. (2014) focused on hypertension medications that are mainly cleared by the kidney in patients with an end-stage renal disease with ADR rate of 12.1% [10].

A study that monitored a plethora of medications for CKD patients over two years concluded that out of 536 patients, 751 adverse drug reactions occurred. 150 ADRs, of which were classified as serious, and 32% of them were considered preventable. Moreover, 16 ADRs caused death, directly or indirectly. The medication ADRs were categorized as follows: Angiotensin-converting enzyme inhibitors (ACEI) or angiotensin-renin blocker (ARB) (15%), diuretics (10%), and antithrombotic agents (14%), in which the later caused 34% of all serious ADRs in the study [11].

Implementing new technology such as computerized physician order entry (CPOE) combined with a clinical decision support system (CDSS) into the healthcare system may have an impact on reducing ADR associated with renal impaired patients suffering from such chronic diseases [7]. Therefore, this study aims to clarify the impact of implementing CDSS and CPOE technology into the healthcare system

environment and preventing ADR in patients suffering from renal insufficiency and diseases by systematically reviewing the literature.

2. Subjects and Methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses checklists and flowcharts in this study. But due to the heterogenicity of the studies included in the review, we were not able to evaluate the biases following PRISMA guidelines

We have mainly included randomized controlled trials (RCT), cohort studies, retrospective, and prospective studies. We performed the search on three databases, including Saudi Digital Library (SDL), PubMed, and Cochrane databases, from 1st January 1990 till October 2020. The search strategy in these databases is presented in Figure 1. We joined the terms CDSS and CPOE together, then combined them with the term renal insufficiency (Renal) and included the terms: Chronic kidney disease CKD, Acute kidney injury (AKI), acute renal failure (ARF), and more. To make the research more concise, we have implemented the most relevant MeSH terms for each of the key concepts in each of the mentioned databases (ig. (("Medical Order Entry Systems"[Mesh]) AND "Decision Support Systems, Clinical"[Mesh]) AND "Renal Insufficiency"[Mesh]). Lastly, the review utilized EndNote X9 to manage the studies and references.

2.1. Study Selection:

We started the systematic review process with 168 articles from three databases (Figure 2). We removed 49 duplicates, after which 119 articles remained for the titles, and abstracts were reviewed. Fifty-eight articles were removed after scanning the title and abstract, and eventually, 61 articles were included in the full-text review. Cohen's kappa coefficient and the Newcastle-Ottawa Quality Assessment Forms (Appendix 1) were used by the two reviewers (H.A and W.A) in the final article selection. In our process, we reached a Cohen's kappa coefficient of 0.55 of interrater agreement, which Cicchetti and sparrow guidelines consider fair. The following table 2 is for the results of the appraisal process:

Table (1) Cohen's kappa coefficient and study appraisal.

		Researcher 1		Calculations	
		Rejected	Approved	Subtotal	Percentage 2
Researcher 2	Rejected	56	1	57	93.5%
	Approved	2	2	4	6.5%
Calculations	Subtotal	58	3		
	Percentage 1	95%	5%	Total = 61	
		(56 + 2) / 61 = 0.95 (95%)			
		(0.95*0.935) + (0.05*0.065) = 0.89 (89%)			
		(Per a – per e) / (1-per e) = 0.55			

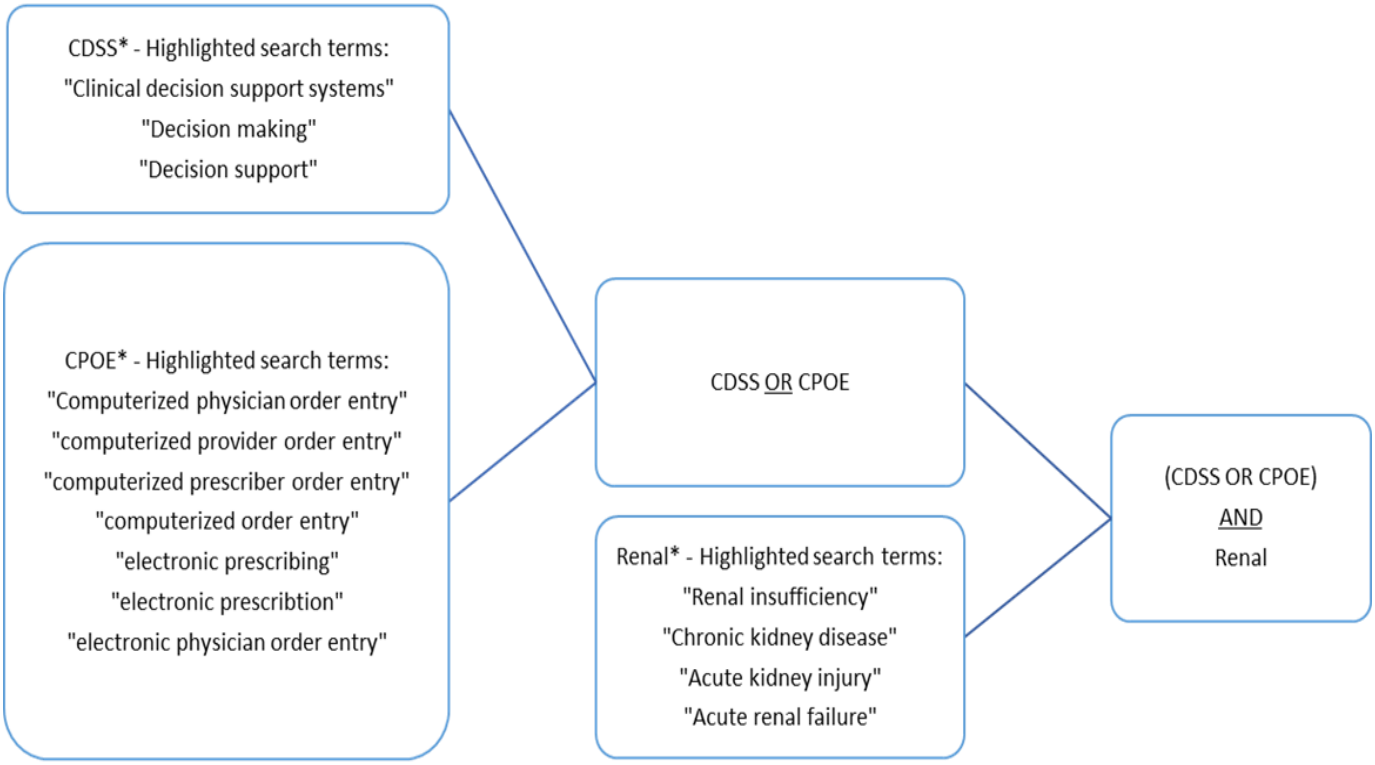

Figure (1) Search strategy used to narrow the search in each of the three databases.

Furthermore, in our study, we followed the PRISMA workflow for study selection as presented in Figure 2 and assessed it against inclusion and exclusion criteria as follows:

Inclusion criteria

1. The studies were randomized controlled trials (RCT), cohort studies, quasi-experimental, alternating time-series, retrospective, and prospective studies.
2. The studies evaluated the effect of CDSS or CPOE on improving medication safety for renal patients.
3. The studies were written in English.

Exclusion criteria

1. The studies did not relate to CDSS or CPOE intervention in renal patients.
2. Duplicate studies.
3. The studies with no full texts available.
4. The studies did not meet the inclusion criteria.

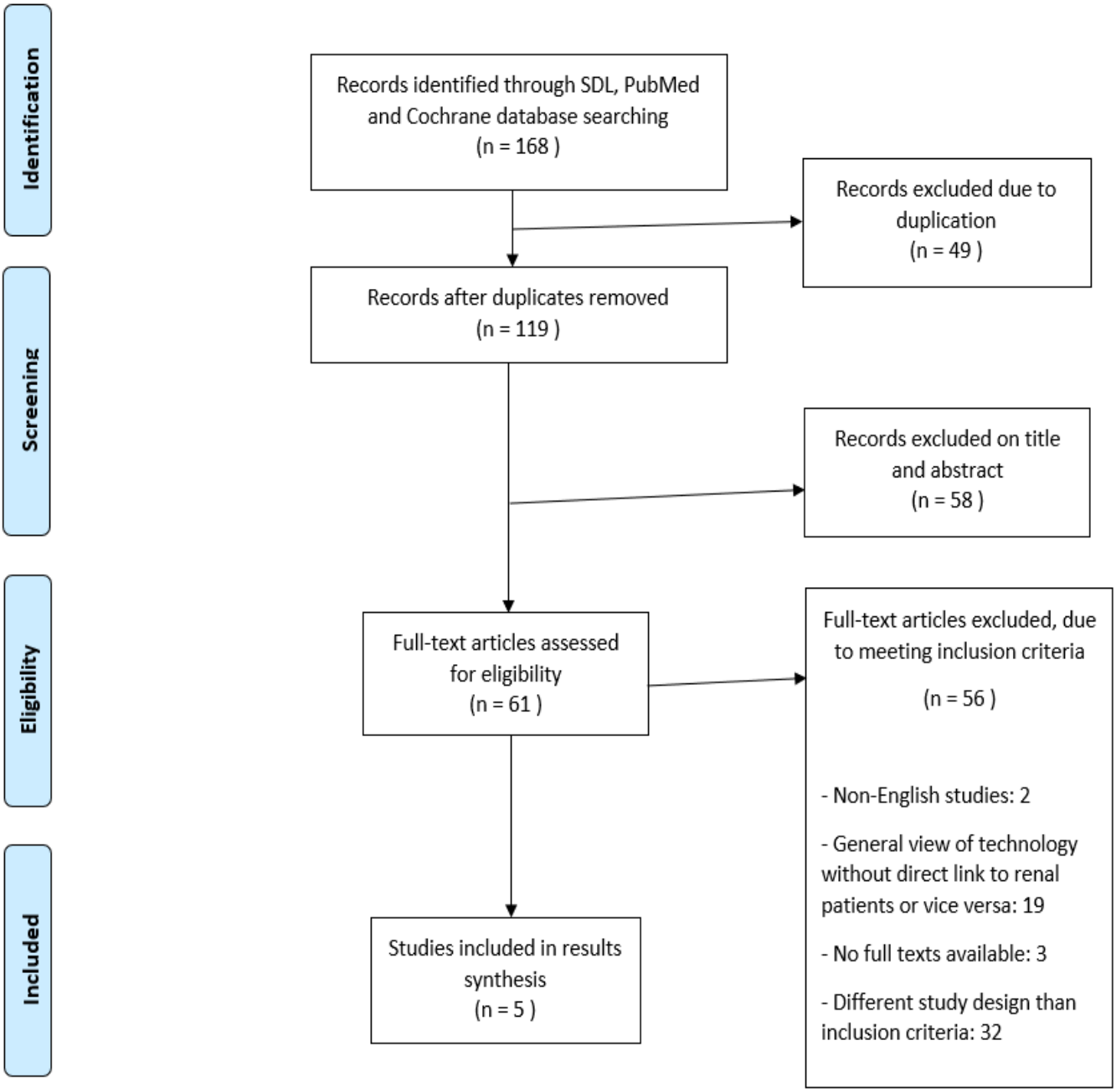

Figure (2) PRISMA workflow for study selection

2.2. Statistical Analysis

We used a narrative synthesis for data results due to the high heterogenicity of the studies included and the lack of reliable data to calculate effect sizes. We mainly developed a theory of the impact of the intervention via the interpretation of data provided in each study narratively. This helps in the identification of gaps in the current research and opens an opportunity for further investigations. We followed the ESRC's: Guidance on the Conduct of Narrative Synthesis in Systematic Reviews [14].

3. Results

In our review, we faced some challenges with the literature due to the specificity of the topic and lack of direct impact on renal patients exclusively. The study designs of most initially collected articles were usually uncontrolled and lacked balance. Five articles out of 168 made it to the final list and are summarized in (Table 2)

Table (2) Characteristics and summary of the included studies

Author, year	Study design	Study population	Sample size	Intervention Outcome	Significant outcomes
P J Helmons et al. 2008 [15]	Retrospective	2752 patients in ICU	n =1788	Nephrotoxic medications were adjusted for 163 patients (86%) with moderate renal failure, and 13 patients (54%) with severe renal failure following CDSS intervention.	Implementing clinical rule-based CDSS can improve appropriate antimicrobial dosing in renal patients.
B Bhardwajaat al. 2011 [16]	RCT	32,917 patients with low eGFR	n= 6125	Nephrotoxic ADR's were significantly lower in the intervention group than in the usual care group (33% vs 49%, p<0.001). When the intervention was expanded to both groups, it resulted in 20% reduction in overall medication errors.	A CDSS was used to alert pharmacists to nephrotoxic medication's errors for patients with renal insufficiency
A A. Leung et al. 2013 [17]	Quasi-experimental	Randomly selected approximately 150 records in each of the 5 hospitals included	n= 1590	45% decrease in the rate of preventable ADE's in renal patients following implementation. Basic CPOE had no significant benefit compared to advanced CDSS (4.6% P=0.87 and 12.4% P=0.01 respectively)	CPOE with advanced CDSS can reduce preventable ADEs. however, it may increase potential ADEs
G Chertow et al. 2001[18]	Alternating time-series	17828 adults admitted to an urban tertiary care teaching hospital	n= 7490	The CDSS intervened in 14440 out of 97151 orders (15%) and required at least 1 parameter to be modified to ensure safety for renal impairment patients by altering dose, frequency, and drug of choice.	CDSS improved and guided proper medication dosing and frequency for renally impaired patients. With no clear advantage over hospitalization costs and reducing length of stay
Kevin M. Terrell et al. 2009 [19]	RCT	The Wishard Memorial Hospital emergency physicians	n= 42 physicians (21 physicians for each of the control and intervention groups)	CDSS provided 73 alerts to ER physicians in the intervention group, who excessively dosed (43%) prescriptions vs a significantly larger proportion of medications (74%) in the control group that was not alerted.	CPOE and CDSS significantly reduced overdosing on medications prescribed by ER physicians. Emergency providers often overlook renal adjustments of medication.

4. Discussion

The systematic review of the literature showed an overall positive impact on preventing ADR's in renal insufficiency patients. Out of the five studies included in this review, 2 studies were RCT, 1 quasi-experimental, 1 retrospective and 1 was alternating time-series. Length of stay (LOS) was also addressed in a study [18] , where it was significantly reduced during the intervention period ($P<0.001$). In contrast, the total costs on both hospital operations and pharmacy were not significantly affected even with the reduction of LOS ($P=0.52$). Terrell et al, (2009) tackled the physician's point of view, where they focused on the hypothesis of overdosing for renal impairment patients usually prescribed by emergency physicians. They showed that the lack of a CDSS can worsen the habit of overdosing on medications that emergency physicians tend to display. We conducted this study to draw attention to the issues on top of the chain usually initiated by the ordering physician and how implementing new, non-hindering technology can increase patient safety [19].

Leung et al. (2013) alluded to the fact that implementing a CDSS into the healthcare environment will essentially increase the safety of patient's care by up to 45%, depending on the level of sophistication of the implemented system. However, these implemented systems will open the possibility for even more ADR's. Their rationale revolves around the idea of the inefficacy of passive alerts where they are often ignored, deferred, or overridden. Alert fatigue is a common issue with implementing new technologies into the hospital system, and these issues, in turn, may increase the chance of ADR's [17]. These concerns promote the need to tailor the CDSS to be as precise and accurate as possible in issuing these alerts.

Lastly, the most critical patients in any healthcare setting are in the intensive care unit (ICU). These patients often express lower levels of renal functions and improving their quality of care directly reflects on their recovery. The CDSS implementation for antibiotic dose adjustment in this study [15] concludes with an overall improvement in antimicrobial dosing in renal failure patients via detecting a high prevalence of unadjusted antimicrobial dosage up to 86%.

Limitations:

Studies included were limited in number and heterogeneous in design, leading to inadequate evaluations. The limited number of selections where due to restrictions in inclusion criteria as we were focusing on quality and relevance to the topic above all. Our search strongly emphasized the need for further quality research on the topic. Other limitations include study limitations to the English language, searching in 3 databases, and some missing articles due inability to acquire them.

4.1 Conclusion

Renal insufficiency patient's protection via implementing new technology received only few quality

research opportunities as demonstrated by our systematic review, even though their importance in ADR avoidance is paramount in any healthcare system. Our systematic review highlighted the positive outcomes of implementing a CPOE coupled with a CDSS in increasing renal patient's safety. However, more quality-controlled studies are needed to evaluate the true impact of these systems protection overall.

5. Declarations

5.1 Abbreviations

CDSS = Clinical decision support system.

CPOE = Computerized physician order entry

ADR = Adverse drug reaction

ADE = Adverse drug events

CKD = Chronic kidney disease

AKI = Acute kidney injury

ARF = Acute renal failure.

ACEI = Angiotensin-converting enzyme inhibitor

ARB = Angiotensin-renin blocker

LOS = Length of stay

ICU = Intensive care unit

ER = Emergency room

5.2 Conflict of Interest Statement

The authors have no conflict of interests to declare.

5.3 Funding Disclosure

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

5.4 Ethical Considerations

None.

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