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LITERATURE REVIEW ON THE APPROPRIATENESS OF MEDICATION PRESCRIPTION IN CHRONIC KIDNEY DISEASE PATIENTS: FOCUS ON ANTIBIOTIC USE

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ABSTRACT

Chronic Kidney Disease (CKD) significantly impacts pharmacokinetics and pharmacodynamics, altering drug metabolism and excretion, thus increasing the risk of drug toxicity. CKD patients are more susceptible to infections, which contribute to significant morbidity and mortality. This underscores the importance of appropriate antimicrobials used in this population. This literature review explores recent findings on medication prescribing practices, dose adjustments, and factors affecting appropriateness, especially in antibiotic use for CKD patients. A comprehensive literature search was conducted using six databases to identify studies published from 2015 to 2024. Twenty-six studies were included. This literature review found that prevalence of inappropriate prescriptions in CKD patients ranges widely between 10% to 77.1% and from 30% to 34,9% specifically for antibiotic, with higher rates observed in outpatient settings compared to hospital environments. Antibiotics, antidiabetic agents, antihypertensive, nutraceuticals, and electrolytes are frequently inappropriately prescribed. Factors influencing inappropriate prescription include comorbidity, severity level of kidney disorder, age, and polypharmacy. The antibiotics most commonly prescribed inappropriately include cefazolin, meropenem, oral sulfamethoxazole-trimethoprim, nebulised colistin, vancomycin, and piperacillin-tazobactam. This study emphasizes the mixed and limited evidence regarding the clinical outcomes of antibiotics dose adjustments in CKD patients. While some studies suggest that antibiotics dose adjustments improve therapeutic outcomes and reduce adverse events, others show no significant impact. Further research is needed to understand the impact of this intervention, as these outcomes may be influenced by various factors. Enhanced education and collaboration between healthcare providers are critical to improving the accuracy of antibiotic prescriptions and ensuring patient safety in CKD management.

KEYWORDS *chronic kidney disease, inappropriate prescription, antibiotics, dose adjustment, clinical outcome, adverse event.*

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INTRODUCTION

Chronic kidney disease (CKD) is characterised as a condition affecting the structure or function of the kidneys, persisting for a minimum of 3 months, and influencing overall health (KDIGO, 2024). CKD is presently a worldwide concern, exhibiting a rising burden and a global median prevalence of 9.5%, which translates to over 700 million individuals afflicted by CKD (Francis et al., 2024), with over 50% of these patients receiving hemolysis treatment (Bello et al., 2024). CKD can induce modifications in pharmacokinetic and pharmacodynamic characteristics that may affect medication exposure and individual treatment responses (Lea-Henry et al., 2018). Individuals with CKD exhibit an increased vulnerability to infections. The increase in infection rates among CKD patients compared to non-CKD patients has been linked to immune system alterations (Ishigami & Matsushita, 2019). Infections resulting from drug-resistant organisms are more prevalent in individuals with CKD. Infections in CKD patients are linked to considerable morbidity and death, necessitating joint preventative strategies, the enforcement of stringent infection control protocols, and the judicious use of antimicrobials to manage infections, especially multidrug-resistant ones (Apata et al., 2021) (Narayanan, 2019) (Zilberman-Itskovich et al., 2022).

Other conditions to consider in CKD patients, include inhibited renal drug excretion, which leads to an extended half-life, prolonged time to achieve steady state, and an increased risk of drug accumulation over time. Furthermore, alterations in volume distribution, particularly those resulting from fluid accumulation, may influence the overall pharmacokinetics of medicines. The decrease in plasma protein binding leads to an increase in the concentration of unbound medicines in circulation, thereby amplifying pharmacodynamic effects and the potential for toxicity. This phenomenon has been documented by (Eyler & Shvets, 2019) and (Vondracek et al., 2021). CKD also influences the metabolism of non-renal medications and modifies the expression of several hepatic enzymes, thereby elevating the risk of drug accumulation and toxicity, particularly in individuals with advanced CKD (Déri et al., 2020; Tan et al., 2018). All of those may influence therapeutic efficacy and raise the incidence of adverse events in CKD patients.

Various groups of drugs, such as antibiotics, ACE inhibitors, ARBs, and NSAIDs, have been proven to elevate the risk of toxicity in individuals with CKD (Clifford et al., 2022). Prior studies indicate that individuals with CKD are susceptible to adverse outcomes, with 32% of these incidents being preventable or potentially preventable. The primary cause of this incidence frequently pertains to the administration of medications with contraindications or dosages inadequately adjusted to the patient's renal function (Laville et al., 2024) thus, drug administration in this population required critical care (Oosting et al., 2024). A comprehensive review of appropriate medication prescribing practices, especially antibiotics for CKD patients, as well as the correlation between prescription appropriateness, therapeutic outcomes, and adverse drug events, remains infrequently reported. This review aims to clarify the recent findings concerning the appropriateness of medication prescribing practices, the frequency of

adjustments, and other factors associated with the appropriateness of medication prescribing, specifically in relation to antibiotic use in patients with CKD.

RESEARCH METHODS

Search Strategy and Sources

The literature search was conducted using LIB UI's e-resources, which included ScienceDirect, Scopus, Taylor & Francis, SpringerLink, and ClinicalKey. Articles were also searched in PubMed as an additional database. The selected keywords were derived from PEO (population, exposure, and outcome). The population is patients with chronic renal disease; the exposure involves antibiotics and inappropriate prescriptions; and the outcomes, although unspecified, encompass prevalence, effectiveness, and adverse medication responses. Furthermore, the reference lists of each included article were thoroughly examined to uncover further studies and confirm the inclusion of all relevant research.

Eligibility Criteria

The selected articles include primary literature published from 2015 to 2024 and articles that defined CKD via creatinine-based equations. Excluded articles are those not in English and do not have open access full text availability.

Screening Procedure

The sreening procedure occurs in two stages. Initially, all articles generated from the preliminary search are screened according to the title and abstract to exclude those that are evidently unrelated. Following the preliminary screening, the complete texts of chosen articles are examined. Articles that fail to meet the eligibility criteria are excluded.

Data Extraction and Reporting

Data extraction was conducted on eligible articles. The extracted data from the articles included study objectives, design, patient criteria, age, gender, sample size, GFR estimation equations used, study results, and details about the country and study setting, aiming to provide a comprehensive overview of the principal findings from the existing literature. The reporting complied with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline.

RESULT AND DISCUSSION

Results of the Literature Search

The research discovered a total of 3,456 entries from six databases, with a screening process applied to 1,152 articles. Subsequently, 16 articles were incorporated into the full-text review process, and 10 additional articles were obtained by examining the reference lists of those publications. A total of 26 publications published between 2015 and 2024 were included according to the specified inclusion and exclusion criteria (Figure 1).

Overview of the included literature

All research included in this study are observational in design. Twelve studies are cross-sectional, eight are cohort studies (six of which employ a retrospective design), one is a case-control study, and five are other types of observational

research. Seventy-three percent of the studies were conducted on hospitalised patients in hospitals (n = 19), while additional studies were performed on outpatient patients in hospitals (n = 2), other outpatient facilities such as primary health care and nephrology clinics (n = 4), and one study examined both hospital and community settings.

The article examines inappropriate medication prescriptions for patients with CKD (n = 17), with three publications primarily focussing on antibiotics and four articles correlating dose precision with therapeutic results and/or adverse drug effects. Three studies examine the knowledge of healthcare professionals, including pharmacists and physicians, concerning appropriate medication prescriptions and dosage suitability for patients with CKD. Additionally, two studies investigate the effects of interventions by healthcare professionals, specifically pharmacists and practitioners, on the quality of medication prescriptions for patients with CKD. Six of the 26 research included thousands of individuals, whereas the remaining studies comprised between 66 and 428 people. The investigations were conducted throughout five continents and seventeen nations, comprising eight studies in Europe, four in Asia, three in America, and two in Oceania and Africa (Table I).

Estimation of Kidney Function and Dose Adjustment in CKD Patients

This review identifies the Cockcroft-Gault equation, the CKD-Epidemiology equation, and the MDRD equation as the most often utilised formulas respectively for assessing the stage of CKD in the examined studies, with three studies employing multiple equations for comparative analysis. This may result from the application of CG equations in clinical trials for dose modification, subsequently incorporated into the product information for pertinent medications during the approval process (Sharma et al., 2022). In clinical practice, employing the MDRD and CKD-EPI equation as a replacement for CG typically yields discrepancies in the assessment of renal function. These differences may have important clinical implications for dose adjustment, particularly when estimated GFR near the cutoff threshold (Castel-Branco et al., 2024).

Although the CG equation was initially referenced in official prescribing guidelines, there remains no agreed-upon standard on which equation to use in cases of discordance. Previous study observed that using the MDRD equation was more likely to result in underdosing. Conversely, most other studies have found the opposite, noting that the MDRD equation often overestimates actual renal function, leading to the prescription of higher drug doses compared to those based on the CG equation (Cox, 2018). However, previous studies have shown that the MDRD and CKD-EPI equations tend to yields similar eGFR values (Al Jasmi et al., 2018). Other study stated that there is a closer alignment of the non-normalized CKD-EPI equation with the CG equation for dosing in CKD patients so that calculating drug dose based on one of these equations is considered acceptable (Khanal et al., 2017).

Meanwhile, other studies conclude that the CG equation should ideally be used as an indicator for amoxicillin and cloxacillin clearance. However, employing entirely different methods, such as therapeutic drug monitoring, could help tailor antibiotic dosages to individual needs (Duval et al., 2022). More studies are needed in the future to identify the most accurate equation for estimating Glomerular Filtration Rate (GFR) in CKD patiens, as GFR estimation is a crucial first step in determining dosages for these patiens. GFR indicates the excretory capacity of the kidneys and is recognised as the most reliable measure for evaluating overall kidney function, as this function typically deteriorates following significant structural damage, with most other renal functions diminishing concurrently with the reduction in GFR values (KDIGO, 2024). Assessing the extent of renal function in patients with CKD is essential for evaluating kidney damage, potential alterations in pharmacokinetics, compromised elimination of toxic metabolites, and the risk of electrolyte imbalances that may result in lethal arrhythmias (Price & Cotten, 2024).

Following the estimation of renal function, the subsequent step in determining dosage for patients with CKD is to align the dosage with the recommended literature. These recommendations actually are provided within the product information but the suggested dosage in product information frequently omits data from post-marketing clinical trials that might substantiate dosing for patients with impaired kidney function. Resources providing drug dose information and primary literature can serve as a more dependable reference in practice, particularly for advanced-stage CKD patients sometimes omitted from initial study (Mirkov et al., 2024). The literature utilized in the studies included in this review comprises the renal medication handbook and electronic resources such as Lexicomp and Micromedex, together with other references in accordance with the guidelines employed at the study site.

Inappropriate Medication Prescription In Patients With CKD

Inappropriate prescribing for patients with CKD is usually defined as the prescription of medications at incorrect dosages or frequencies, as well as those that are contraindicated due to the patient's renal function (O'Shaughnessy et al., 2017). In a separate study, an inappropriate drug dosage is explicitly defined as a medication prescribed at a level that deviates from the suggested dosage in the literature, either exceeding or falling short of it; other studies solely classify it as a dosage that is excessively high. Also a medicine that should be avoided is one that is used with caution in patients with chronic renal disease. Concurrently, another study investigates the suitability of drug dosages given to patients with chronic renal disease.

The incidence of inappropriate medicine prescriptions for patients with CKD varies between 10% and 64.7% in hospitals. Antibiotics, antidiabetes (metformin, glibenclamide, sitagliptin, gliclazide), antihypertension (spironolactone, captopril,

enalapril, hydrochlorothiazide, losartan, ramipril, bisoprolol, furosemide), simvastatin, allopurinol, tramadol, aspirin, domperidone), nutraceuticals, and electrolytes are some of the medicines that are often wrongly prescribed to people with CKD (Sönnerstam et al., 2016) and reaches 77.1% in other healthcare settings, such as primary health clinics (Ruiz-Boy et al., 2022). At a nephrology clinic, the prescription error rate is 66%, with 31% of prescriptions containing contraindicated medications and 35% prescribed at elevated levels (Laville et al., 2018). This review determined that the incidence of inappropriate medication prescriptions in CKD patients is diminished in hospitals relative to other non-hospital healthcare settings. This might have something to do with better monitoring in hospitals, specifically the regular checking of renal function indicators that help with the ongoing review of the risk-benefit ratio of drug treatments (Arcoraci et al., 2021).

The accuracy of prescriptions resulting from incorrect dosages varies between 26.8% and 56.1% (Hayat et al., 2023). In trials focused on antibiotics, the incidence of dosage errors in patients with CKD was found to be lower, ranging from 30% to 34.9%. However, studies that weren't specifically about antibiotics found that vancomycin, ceftazidime, cefixime, cotrimoxazole, ciprofloxacin, colistin, cefazolin, and meropenem are the most commonly prescribed drugs, even though their dosages are different from what the literature suggests for people with CKD .

Factors Affecting Inappropriate Medication Prescription In Patients With CKD Comorbidity

The precision of prescriptions for patients with CKD is markedly associated with the existence of comorbidities (Birarra et al., 2022). According to Hayat et al., 2023, people with CKD who also have high blood pressure, diabetes mellitus, or cardiovascular disease are respectively 2.68 times, 3.47 times, and 2.82 times more likely to get higher doses. Patients with CKD and comorbidities are reported to be 6.31 times more likely to be prescribed nephrotoxic drugs (95% CI: 2.01–19.79).

Severity level of kidney disorders

A notable link exists between the severity of renal insufficiency and the incidence of inappropriate medication prescriptions ($P = 0.02$, $r = 0.056$) (Yang et al., 2016). According to the literature, prescription adherence to the literature was found to be lower in patients with severe kidney impairment (46.0%) than in those with moderate kidney impairment (58.1%, RR 0.79; 95% CI 0.70-0.89). Because of this, people with stage 5 CKD are much more likely to get the wrong prescriptions, even after getting full nephrology treatment (Alqashqri et al., 2024) and people with lower GFR are 10.2 times more likely to get the wrong prescriptions (95% CI 6.02; 17.30).

Age

The chance of getting the inappropriate prescription goes up with age for people with CKD (AOR = 1.12, 95% CI: 1.07–1.17) (Zeleke et al., 2024). People over 60 years old with CKD have a higher chance of getting the wrong medicines (OR = 9.49) than people between the ages of 41 and 60 (OR = 5.76).

Polypharmacy

The likelihood of obtaining an inappropriate prescription escalates 1.43 times (95% CI: 1.05–1.93) in patients with CKD as the quantity of prescribed drugs rises. Patients prescribed 11 drugs are 5.88 times more likely to receive an erroneous prescription than those prescribed fewer than five prescriptions. The rising quantity of drugs administered at hospital admission elevates the probability of inappropriate prescribing for CKD patients (OR 1.1, 95% CI 1.02–1.18, p = 0.010).

These factors actually are interrelated and complicate the prescription of medication in patients with CKD. Individuals with CKD may concurrently exhibit 1 to 3 comorbidities. People who have CKD often have problems with their musculoskeletal system and high blood pressure. As the person gets older and the kidney disease gets worse, they may also have more problems with their heart and diabetes. According to recent studies by Chen et al., 2024 and MacRae et al., 2021, this condition exacerbates the drug load on patients, as clinical guidelines predominantly concentrate on individual diseases, frequently presenting contradicting recommendations among those conditions. Because of this, people with CKD often have complicated treatment plans that include a lot of different drugs. For example, a study found that people with CKD who also had other health problems were given an average of 9 drugs every day.

Patterns of antibiotic utilisation in patients with CKD

According to the search results, three studies examine the pattern of antibiotic utilisation in individuals with CKD. All three investigations delineate the pattern of antibiotic utilisation in patients receiving haemodialysis. The predominant infections in hospitalised CKD patients include respiratory tract infections, skin and soft tissue infections, bloodstream infections, urinary tract infections, and vascular access infections. This data aligns with other studies indicating five types of infections prevalent among CKD patients. Meanwhile, the most prevalent infection among outpatients is skin infection. The predominant antibiotics given for therapeutic purposes comprise 35% empirical antibiotics. Currently, the prescription rate of antibiotics without a confirmed infection diagnosis stands at 32.42% among outpatients. The rate of antibiotic prescriptions per 1,000 patients is 520.29 for end-stage CKD patients and 296.48 for non-CKD patients, indicating that the former group receives nearly twice the amount of antibiotics compared to the latter. These findings underscore the importance of appropriate antibiotic

management in CKD patients, limiting use to clinical indications to reduce the risk of antibiotic resistance in this population. CKD patients are more susceptible to Multi Drug Rresistance organism (MDRO) infections, with repeated antibiotic exposure being a primary factor in resisctance development.

The antibiotics most frequently prescribed in CKD patients are vancomycin, piperacillin-Tazobactam and ceftriaxone. The most frequently administer at inappropriate dosages include cefazolin, meropenem, sulfamethoxazole-trimethoprim (oral), and colistin (nebulised) (Table II). The predominant cause of inaccuracy is an excessively high dose or an insufficient dosing interval (Figure II). The prevalence of inappropriate vancomycin prescriptions differs among studies, with the initial study indicating that nearly all prescribed vancomycin regimens were deemed appropriate, while only three regimens were classified as inappropriate due to dosing frequency lacking reference to therapeutic drug monitoring (TDM). Among the three inappropriately administered vancomycin regimens, therapeutic drug monitoring was unavailable for two of them. In the second investigation, vancomycin emerged as the most frequently administered antibiotic with an erroneous dosage. The third study revealed that up to 36% of sulfamethoxazole-trimethoprim prescriptions were administered at elevated doses to individuals with CKD.

Inappropriate vancomycin dosing in CKD patients raises the risk of Acute Kidney Injury (AKI), especially when combined with other nephrotoxic drugs, accelerating CKD progression and increasing cardiovascular risk. In ESRD, central vascular access heightens sepsis risk with high mortality rates, largely due to MRSA infections. Appropriate vancomycin dosing is essential to prevent pathogen resistance and preserve remaining kidney function. Research indicates that inappropriate sulfamethoxazole-trimethoprim dosing in CKD patients can heighten the risk of crystalline nephropathy. Close monitoring, dose adjustments, and hydration, potentially with urine alkalinization are essential to improve crystal solubility and reduce risks. Other research suggest that high dose administration of sulfamethoxazole-trimethoprim, particularly when co-administered with other nephrotoxic agents, constitutes a risk factor for acute kidney injury, even in individuals with baseline normal kidney function. A case report describes a 65 years old female with ESRD on hemodialysis who developed tonic-clonic seizures after receiving the standard meropenem regimen for pyelonephritis. Seizures ceased upon drug discontinuation, highlighting a possible risk of neurotoxicity associated with standard dosing. Additional study found a significant correlation between renal function and meropenem concentration, patients with moderate to severe renal impairment demonstrated elevated meropenem concentrations with decreased clearance, even at reduced dosing. In contrast, hyperfiltrating patients despite

receiving the highest meropenem doses, exhibited the lowest serum concentrations, of the below the PK/PD target threshold.

Clinical outcome associated with dosage adjustment in CKD patients

Antibiotic doses that are not adjusted according to the kidney function of patients with CKD are at risk of causing adverse drug reactions. On the other hand, to this day, the benefits of adjusting antibiotic doses in patients with CKD remain controversial. This intervention aims to achieve the necessary antibiotic exposure, so that the effectiveness of the therapy can be reached while reducing toxicity. Recent studies report that there is still very little high-quality evidence regarding the recommended dose reduction for antibiotics in patients with CKD. In line with those findings, studies on the relationship between antibiotic dosage appropriateness and clinical outcomes such as therapy effectiveness and adverse drug reactions remain very limited in this review. These limitations include the study being restricted to only one type of infection, one type of antibiotic, and a specific patient population, which means that generalizing the research results must be done with caution. Another very important factor to consider in antibiotic dose adjustment is ensuring that the dose adjustment recommendations can optimize antibacterial activity. Antibiotics exhibit pharmacodynamic activity that is dependent on concentration or time, so administering smaller doses can maintain a more stable drug concentration and is therefore preferred for antibiotics whose activity depends on time. In contrast, antibiotics whose activity depends on concentration may be better suited to extending the dosing interval to maintain high peak concentrations and low trough concentrations.

Based on the results of the investigation, studies regarding the relationship between dose appropriateness and therapy outcomes focus on examining outcomes related to therapy effectiveness and adverse events. The results found among studies vary, making it difficult to conclude the relationship between dose appropriateness and antibiotic therapy outcomes to date. One study reported no relationship between dose adjustment and therapeutic improvement, or in other words, no significant difference between the adjusted and non-adjusted groups regarding therapeutic outcomes. On the contrary, two other studies reported differently. Patients with CKD treated in the intensive care unit are 2.23 times more at risk of experiencing therapy failure and 2.29 times more at risk of death after receiving antibiotic doses adjusted for kidney function. Although this study explains that therapy failure is closely related to mortality in patients, other factors such as the severity of the infection and the occurrence of sepsis/septic shock also influence patient outcomes. Other study have also shown similar results, where the clinical response of CKD patients receiving antibiotics without dose adjustments was recorded to be 4.02 times better compared to the adjusted group. This group also experienced a lower therapy failure rate, although it was only 6%. However,

no significant differences were found in mortality rates between the groups. In general, it has been reported that there is no difference in clinical outcome between dose-adjusted and non-dose-adjusted CKD patients.

The class of drugs most frequently associated with adverse events leading to hospital admissions in patients with CKD includes antithrombotic agents, such as antiplatelet and anticoagulant medications, as well as nonsteroidal anti-inflammatory drugs (NSAID). This class of medication is reported to frequently cause gastrointestinal disturbances, metabolic and nutritional disorders such as hypoglycemia, hyperkalemia, hyponatremia, and dehydration, as well as blood and lymphatic system disorders such as microcytic anemia and bone marrow toxicity, which have been reported as the most common adverse events in patients with CKD. The adverse events observed with the use of adjusted cefoperazone-sulbactam in CKD patients include diarrhea ($p = 0.326$), eosinophilia ($p = 1.000$), prolonged prothrombin time ($p = 0.674$), alterations in kidney function ($p = 0.938$), and leukopenia ($p = 0.938$). Meanwhile, in tuberculosis medications, there are hepatitis and skin reactions, and these events are influenced by the severity of kidney function impairment. However, both studies found that the incidence of adverse events in dose-adjusted and non-dose-adjusted groups among CKD patients did not differ significantly. Support for this finding comes from other research showing no relationship between the administration of non-adjusted drug doses in CKD patients and hospital admissions due to adverse events. This finding is consistent with the observation that the majority of hospitalizations due to adverse events in CKD patients are not caused by incorrect dosing. In addition, the clinical outcomes of patients may be influenced by other variables, thus requiring studies with a prospective and controlled design to gain a deeper understanding of the impact of dose adjustments on clinical results.

Knowledge and Impact of healthcare providers intervention in dose adjustments for CKD patients

Studies on this topic conclude that medical students, physician, and pharmacists still have a level of knowledge that needs to be maximized regarding dose adjustments for patients with kidney function disorders. Physicians demonstrated better performance in classifying medications that require dose adjustments compared to students, although errors still occur frequently, particularly in avoiding high-risk drugs that can lead to adverse drug reactions and side effects. Pharmacists generally possess adequate knowledge, especially those working as clinical pharmacists, but still face obstacles such as a lack of patient data and incomplete medical histories. This is in line with findings from another study that focused on assessing the knowledge of pharmacists working in a hospital. The majority of pharmacists demonstrated good dose adjustment practices for patients with CKD. These findings highlight the importance of enhancing continuing

education to increase knowledge and clinical practices related to medication dose adjustments in order to improve safety and quality of care for patients with CKD.

Two studies in this review observed the impact of healthcare interventions, such as those by nephrologists and pharmacists, on the appropriateness of medication dosing received by patients with CKD. The first study examined the effects of collaborative care between general practitioners and nephrologists for CKD patients. This research found that the majority of antibiotic prescriptions given by general practitioners to patients with stage 4 and 5 CKD did not align with the recommended dosages in the literature, and only 30% of patients without collaborative care from a specialist received the correct antibiotic dosage. Collaborative care with nephrologists was found to increase adherence to antibiotic prescribing with dosages that matched literature recommendations by 34%, and patients receiving collaborative care were 1.2 times more likely to receive dosages in accordance with recommendations compared to those who only received care from general practitioners (95% CI = 1.09 – 1.32, p <0.001). Another study examined the impact of pharmacist interventions on outpatient CKD patients at a hospital; findings showed that out of 302 medication dosage adjustment recommendations made by pharmacists to 269 CKD patients, 72.52% were accepted by physicians. The medications most frequently adjusted in dosage include levofloxacin (8.94%), metformin (5.29%), and amoxicillin-clavulanate (5.29%). Both finding emphasize the need for enhanced education, collaboration, and vigilance in adjusting medication dosages to reduce the risk of side effects and improve the safety of patients with CKD.

CONCLUSION

This literature review outlines the latest findings from studies discussing the inappropriate of drug prescribing in patients with CKD. The prevalence of inappropriate prescribing ranges from 10 – 64,7% in hospitals and up to 77,1% in outpatient facilities, especially for antibiotic, the incorret dosage prescription ranges widely from 30% to 34,9% depending on the specific antibiotic. Factors that associated with inappropriate prescribing in CKD patients include comorbidities, severity of kidney impairment, age and polypharmacy. Antibiotics, antidiabetes, antihypertension, simvastatin, allopurinol, tramadol, aspirin, domperidone, nutraceuticals, and electrolytes are some of the medicines that are often inappropriately prescribed to CKD patients. The antibiotics most frequently prescribed inappropriately include cefazolin, meropenem, sulfamethoxazole-trimethoprim (oral), colistin (nebulised), vancomycin and piperacillin-tazobactam. The predominant cause of inappropriatness is an excessively high dose or an insufficient dosing interval. However the relationship between dose adjustment and antibiotic therapy outcome remains difficult to determine due to the limitation and

lack of study. Strenghtening continuing education to improve knowledge and clinical practices, improving collaboration among healthcare providers, and ensuring careful monitoring are essential to minimise the risk of side effects, ensure patient safety and achieve optimal therapeutic outcome in CKD patients

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