

Role of Pharmacist in Pediatric Dosage Adjustments for Renal Impairment

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Abstract:

Pharmacists play a critical role in ensuring safe and effective medication use in pediatric patients, particularly those with renal impairment, where renal function significantly influences drug pharmacokinetics and pharmacodynamics. Given the physiological differences between children and adults, as well as the variability in renal maturation, pharmacists must assess the patient's renal function using appropriate formulas, such as the Schwartz equation. Furthermore, pharmacists evaluate the specific drug characteristics, including elimination pathways, potential nephrotoxicity, and age-specific dosage guidelines. Their expertise allows them to provide tailored dosing recommendations and monitor therapeutic outcomes, ensuring that children receive appropriate medication without increasing the risk of adverse effects. In addition to dosage adjustments, pharmacists also serve as vital resources for educating healthcare providers and caregivers about the implications of renal impairment on medication therapy. This includes highlighting the importance of adherence to dosing schedules, potential side effects, and the need for regular monitoring of renal function. By collaborating with healthcare teams, pharmacists can help develop comprehensive care plans that prioritize safety while maximizing therapeutic efficacy. Their involvement is crucial in clinical decision-making, ultimately leading to improved health outcomes for pediatric patients with renal impairment.

Keywords: Pediatric pharmacy, Dosage adjustments, Renal impairment, Pharmacokinetics, Schwartz equation, Nephrotoxicity, Therapeutic monitoring, Medication safety, Healthcare collaboration, Patient education.

Introduction:

The proper management of pediatric patients poses unique challenges in the realm of pharmacotherapy, primarily due to their distinct physiological differences compared to adults. Among these challenges, the issue of renal impairment is particularly significant, as it can profoundly affect drug pharmacokinetics and pharmacodynamics in children. The kidneys play an essential role in drug clearance, and any compromise in their function necessitates careful consideration of dosage adjustments. As the front-line healthcare professionals who bridge the gap between medicine and patient care, pharmacists assume a critical role

in managing dosage adjustments for pediatric patients with renal impairment. This introduction delves into the multifaceted responsibilities of pharmacists in this context, highlighting the complexities of pediatric dosing, the implications of renal function on pharmacotherapy, and the collaborative efforts required among healthcare providers to optimize patient outcomes [1].

Pediatric patients are not simply smaller versions of adults. Their immature organ systems, including those responsible for drug metabolism and excretion, significantly influence how medications are processed within their bodies. Renal function in infants and children continues to mature over the

first several years of life, affecting drug pharmacokinetics — the absorption, distribution, metabolism, and excretion (ADME) of medications. This maturation process complicates the approach to prescribing medications, particularly for those with renal impairment, which can arise from congenital anomalies, infections, or other underlying health conditions such as diabetes or hypertension. Clinical guidelines for drug dosing often rely on age, weight, or body surface area; however, these factors may not adequately account for individual variations in renal function [2].

The pharmacokinetic changes associated with renal impairment can lead to increased serum drug levels, prolonged half-lives, and heightened risk of toxicity, particularly for renally-excreted medications. In pediatric patients, small errors in dosing can lead to significant adverse effects due to their lower body reserves and differing metabolic capacity. Therefore, clinicians must adjust dosages based on not only the severity of renal impairment as assessed by creatinine clearance or glomerular filtration rate (GFR) but also consider the unique developmental considerations and metabolic profiles of the pediatric population [3].

Pharmacists are instrumental in the clinical decision-making process regarding the safe and effective use of medications in children, especially those with renal impairment. Their expertise in pharmacotherapy, attention to detail, and comprehensive understanding of drug interactions enable them to provide invaluable guidance in determining appropriate dosing adjustments. In many healthcare settings, pharmacists play a pivotal role in medication reconciliation, assessing renal function, and advising on potential nephrotoxicities that could exacerbate existing renal impairments. Furthermore, as members of multidisciplinary healthcare teams, pharmacists collaborate with physicians and nurses to ensure that medication regimens are individualized, effective, and safe for pediatric patients [4].

The role of the pharmacist is not limited to acute care settings; it extends to outpatient environments, where chronic renal conditions often necessitate ongoing medication management. In this capacity, pharmacists contribute to patient and caregiver education about the importance of adherence to prescribed dosages and the recognition of adverse drug reactions that may indicate worsening renal function or toxicity. They also foster an environment

where careful monitoring of renal parameters and medication efficacy becomes standard practice [5].

Additionally, the evolving landscape of pediatric pharmacotherapy necessitates a commitment to research and knowledge transfer within the pharmacist community. Despite the growing body of literature on pediatric pharmacokinetics, much remains to be learned about the nuances of renal dose adjustments across different age ranges and specific disease states. Continuous professional development in this area enables pharmacists to stay informed and equipped to advocate for best practices in medication management for children with renal impairment [6].

Understanding Renal Impairment in Pediatric Populations:

The kidneys are vital organs responsible for numerous critical functions, including the regulation of electrolyte balance, blood pressure control, regulatory filtration of metabolic waste products, and the maintenance of acid-base homeostasis. Unlike adults, children possess unique anatomical and physiological characteristics that necessitate a distinctive approach when examining renal impairment [7].

Before delving into renal impairment, it's essential to understand the basic renal physiology in children. The kidneys of neonates and infants differ significantly from those of older children and adults in terms of size, developmental stage, and functional capacity. In the very young, glomerular filtration rate (GFR) is significantly lower compared to that of older children, reaching adult levels by the age of two. This infantile renal system undergoes substantial maturation that impacts fluid and electrolyte management, making pediatric patients more susceptible to fluctuations in hydration and electrolyte balance during acute illnesses [7].

The nephron, the functional unit of the kidney, continues to develop postnatally, with nephron number peaking around the age of 36 weeks' gestation and remaining relatively stable thereafter. Factors such as low birth weight and gestational age can alter nephron numbers, leading to predispositions for renal disease later in life.

Renal impairment in pediatric populations arises from diverse etiologies, including congenital anomalies, acute injuries, chronic diseases, and hereditary conditions. Among the congenital causes,

renal dysplasia, polycystic kidney disease, and obstructive uropathy rank prominently [8].

Acute renal injury (AKI) can occur due to various pre-renal, intra-renal, and post-renal factors. Prerenal causes typically result from diminished renal perfusion, often due to dehydration, shock, or congenital heart defects. Intra-renal causes primarily relate to intrinsic damage to renal parenchyma from conditions such as glomerulonephritis, hemolytic uremic syndrome, and nephrotoxic exposures. Post-renal causes, though less common, involve obstructive processes, including kidney stones or enlarged urinary tracts secondary to anatomical abnormalities [9].

Chronic renal failure (CRF) in children can stem from a multitude of factors. The leading causes include congenital anomalies of the kidney and urinary tract (CAKUT), chronic glomerulonephritis, metabolic disorders, systemic diseases like lupus nephritis, and inherited disorders such as Alport syndrome. The prevalence of kidney disease in pediatric patients underscores the need for comprehensive awareness surrounding congenital and acquired factors in renal health [10].

Diagnosing renal impairment in children involves a multi-faceted approach that starts with a comprehensive clinical history and physical examination. Emerging symptoms such as reduced urine output, changes in urine color, swelling, hypertension, or signs of growth failure warrant further investigation.

Clinical laboratory tests, including serum creatinine, electrolytes, and urinalysis, are integral to assessing kidney function. An elevated serum creatinine level indicates impaired glomerular filtration rate, while urinalysis can reveal hematuria, proteinuria, and electrolyte abnormalities, contributing important diagnostic information. Imaging studies, such as renal ultrasounds, can elucidate structural anomalies and assess kidney size and urinary tract obstructions [11].

In certain cases, renal biopsy may be indicated to characterize specific glomerular diseases when conservative measures are inadequate. This invasive procedure allows for histological evaluation and aids in developing targeted therapeutic strategies [11].

Renal impairment in pediatric populations presents with diverse clinical manifestations, which can vary depending on the age of the child and the aetiology of the impairment. Common symptoms include a

marked decrease in urine output, swelling due to fluid retention, hypertension, electrolyte imbalances, and changes in metabolic waste products leading to uremia.

Children with renal impairment may exhibit growth retardation, a significant concern due to its profound implications on physical and cognitive development. Additionally, because pediatric renal disease can affect multiple organ systems, the manifestations of renal impairment may be multi-systemic, complicating clinical presentation further [12].

Cognitive functions may also suffer due to the accumulation of waste products, leading to significant impacts on school performance and overall quality of life. Psychology, growth, nutrition, and familial impacts must all be part of a holistic management plan.

Managing renal impairment in children necessitates a patient-centered approach that considers the underlying cause of the condition, the severity of renal impairment, and the child's overall health status. Immediate management of acute renal injury generally involves fluid management, correction of electrolyte imbalances, and addressing the etiology of the renal insult [12].

In cases of chronic renal disease, management includes controlling blood pressure, managing associated comorbidities like diabetes, and monitoring growth and development closely. Dietary modifications may be needed to limit protein and electrolyte intake, and in severe cases, pharmacotherapy may be warranted to control symptoms, manage anemia, and complement renal function [13].

For children with end-stage renal disease, options include dialysis and renal transplantation. The decision for either intervention is complex, requiring extensive consideration of the child's medical history, family dynamics, and socioeconomic factors [13].

The long-term effects of renal impairment in pediatric populations are profound and can have lasting implications. Children with chronic kidney disease (CKD) face risks of cardiovascular disease, bone mineral disorders, and psychosocial challenges, underscoring the critical need for lifelong monitoring and intervention [13].

Developmental delays, both in physical growth and cognitive functions, can persist into adolescence and adulthood, making early diagnosis and efficient

management proscribed paramount. Pediatric nephrology thus plays a crucial role in establishing protocols for transition to adult care to continue vigilant oversight of renal health [13].

Pharmacokinetics and Pharmacodynamics in Renal Impairment:

The principles of pharmacokinetics and pharmacodynamics are crucial in the development and administration of therapeutic drugs. Pharmacokinetics refers to the study of how the body absorbs, distributes, metabolizes, and excretes drugs, whereas pharmacodynamics focuses on the biochemical and physiological effects of drugs and their mechanisms of action. In patients with renal impairment, both pharmacokinetics and pharmacodynamics can be significantly altered, necessitating careful consideration during medication management to ensure efficacy and minimize toxicity [14].

The kidneys play a pivotal role in maintaining metabolic homeostasis by filtering blood, excreting waste products, regulating electrolyte balances, controlling blood pressure, and maintaining acid-base equilibrium. As key organs in drug elimination, the kidneys are integral in determining a drug's pharmacokinetics. Renal impairment, which can range from mild dysfunction to complete renal failure, has significant implications for drug disposition. Causes of renal impairment may include acute kidney injury (AKI), chronic kidney disease (CKD), and established end-stage renal disease (ESRD). Each of these conditions presents unique challenges for drug dosing and effectiveness [14].

Pharmacokinetics in Renal Impairment

1. **Absorption:** In general, the absorption of orally administered drugs is not significantly altered by renal impairment. However, certain factors related to kidney dysfunction, such as gastrointestinal motility and the presence of metabolic acidosis, can influence the absorption of specific medications. For instance, altered gut flora in patients with renal failure can affect the bioavailability of certain drugs [15].
2. **Distribution:** The distribution of drugs is influenced by various factors, including plasma protein binding and body composition. Renal impairment can lead to changes in protein binding, particularly in

drugs that are highly bound to serum albumin. In CKD or ESRD, decreased levels of albumin and other binding proteins may result in an increased free fraction of the drug, which can enhance its pharmacologic effects and toxicities. Additionally, fluid retention often observed in renal dysfunction can alter the volume of distribution, particularly for water-soluble medications [15].

3. **Metabolism:** The liver is primarily responsible for drug metabolism, but the kidneys also contribute, especially for the metabolism of certain drugs and their active metabolites. Renal impairment can affect hepatic blood flow, enzyme activity, and the overall metabolism of drugs. Although most drug metabolism occurs in the liver, clinicians must be cautious of the role that the kidneys play in the activation and inactivation of certain pharmacologically active compounds [16].
4. **Excretion:** The most critical influence of renal impairment on pharmacokinetics is in the excretion phase. The kidneys are responsible for the elimination of various drugs and their metabolites via glomerular filtration, tubular secretion, and reabsorption. In patients with renal impairment, a reduced glomerular filtration rate (GFR) leads to decreased clearance of renally-excreted drugs. As a result, these drugs can accumulate in the body, resulting in potential toxicity. Drugs such as aminoglycosides, digoxin, lithium, and certain nonsteroidal anti-inflammatory drugs (NSAIDs) are particularly susceptible to accumulation and require careful dose adjustments based on renal function [16].

Pharmacodynamics in Renal Impairment

Pharmacodynamics refers to the relationship between drug concentration and effect. Renal impairment can alter both the efficacy and toxicity of medications through several mechanisms:

1. **Altered Drug Receptor Interactions:** Changes in the number or affinity of drug receptors can influence the pharmacodynamic response. For instance, the sensitivity of beta-adrenergic receptors may be altered in patients with renal

failure, impacting the effects of beta-agonists or antagonists [17].

2. **Homeostatic Balance:** With impaired renal function, the body's ability to maintain homeostasis is compromised, affecting the pharmacodynamic responses of certain drug classes. Electrolyte imbalances, fluid overload, and acid-base disturbances can lead to altered pharmacological effects, especially with diuretics, antihypertensives, and drugs acting on the central nervous system.
3. **Toxicities and Side Effects:** Patients with renal impairment are more susceptible to the side effects of various medications due to altered pharmacodynamics. For example, the accumulation of uremic toxins and the disturbance of electrolyte levels in CKD can exacerbate the cardiotoxicity associated with certain drugs, such as digoxin [17].

Clinical Considerations and Implications

Given the significant implications of renal impairment on pharmacokinetics and pharmacodynamics, clinicians must employ a comprehensive strategy for managing medication in affected patients. Key considerations include:

- **Assessing Renal Function:** Regular evaluation of renal function using estimated GFR (eGFR) and serum creatinine is critical in guiding dosing decisions for renally eliminated drugs. Tools such as the Cockcroft-Gault formula or the Modification of Diet in Renal Disease (MDRD) equation can help estimate kidney function [18].
- **Dose Adjustments:** Medication dosing regimens often require modification based on renal function. This can include adjusting the dose, extending the interval between doses, or selecting alternative agents that are less reliant on renal clearance.
- **Monitoring:** Regular therapeutic drug monitoring is essential, particularly for drugs with narrow therapeutic indices, to prevent toxicity and ensure therapeutic efficacy.

- **Patient Education:** Patients should be counseled regarding the importance of adhering to their prescribed regimens, recognizing signs of drug toxicity, and understanding the potential need for dosage adjustments in relation to changes in renal status [18].

Assessment of Renal Function: Tools and Techniques:

The kidneys play a fundamental role in the body's homeostasis, responsible for the filtration of blood, elimination of waste, regulation of electrolyte levels, and maintenance of acid-base balance. Assessment of kidney function is critical for the diagnosis and management of various renal disorders, as well as for the safe use of many medications that are cleared through the kidneys. Considering the intricate relationship between kidney function and pharmacotherapy, the role of the pharmacist in kidney function evaluation cannot be overstated [19].

Kidney function primarily hinges on the glomerular filtration rate (GFR)—an indicator of the kidneys' ability to filter blood. Normal GFR values fluctuate based on age, sex, and body size, with the average range being between 90 and 120 mL/min/1.73 m² for healthy adults. A decrease in GFR can signal impaired kidney function, necessitating a careful evaluation of renal health and tailored therapeutic interventions [19].

Tools and Techniques for Evaluating Kidney Function

Several methods exist for evaluating kidney function, each with its advantages and drawbacks. Commonly used techniques include serum creatinine measurement, urinary tests, and estimates of GFR through equations and measurement of creatinine clearance [20].

1. **Serum Creatinine Test:** Serum creatinine is a byproduct of muscle metabolism, produced at a relatively constant rate and cleared primarily by the kidneys. A serum creatinine test, although a cornerstone in assessing renal function, has limitations. It does not reflect acute changes in kidney function because it typically stabilizes several hours after a drop in GFR occurs. Additionally, factors such as age, gender, muscle mass, and diet can influence creatinine levels, potentially leading to

misinterpretations in certain patient populations, notably the elderly and those with low muscle mass [21].

2. **Estimation of GFR (eGFR):** To address the limitations of serum creatinine, multiple equations have been developed to estimate GFR. The most widely employed formulas include the Cockcroft-Gault equation, the Modification of Diet in Renal Disease (MDRD) Study equation, and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Among these, the CKD-EPI equation is currently favored in many clinical settings due to its ability to provide a more accurate reflection of kidney function across diverse populations [22].
3. **Creatinine Clearance Test:** This method involves measuring the amount of creatinine in a 24-hour urine sample and correlating it to serum creatinine levels to calculate the creatinine clearance rate. While this can give a more precise measurement of renal function, it is cumbersome and prone to inaccuracies due to incomplete collections.
4. **Urinalysis:** Beyond measuring creatinine, urinalysis can provide insights into kidney health through the assessment of protein, glucose, and blood in urine. The presence of protein (proteinuria) can indicate kidney damage, while glucose (glycosuria) may suggest diabetic nephropathy.
5. **Imaging Studies:** Techniques such as ultrasound and CT scans can visualize kidney structure and function, identifying abnormalities such as obstructions, stones, or tumors that could affect renal performance. These imaging modalities are particularly useful in cases where obstructive uropathy or structural anomalies are suspected [22].

The Role of the Pharmacist in Kidney Function Evaluation

Pharmacists play a pivotal role in the comprehensive care of patients, particularly concerning the implications of kidney function on drug therapy. With medications being processed through the kidneys, understanding the nuances of renal function is vital for preventing adverse drug reactions. In

several key areas, pharmacists can enhance patient care related to kidney function:

1. **Medication Management:** Pharmacists are crucial in ensuring that medication dosages are adjusted appropriately for patients with varying degrees of renal impairment. Many drugs require dose recalibration based on the eGFR to avoid toxicity. Through renal function assessments, pharmacists can recommend dosage adjustments and monitor therapeutic levels of medications that exhibit nephrotoxicity [23].
2. **Patient Education:** Educating patients about the importance of renal health, medication adherence, and lifestyle modifications can significantly influence outcomes. Pharmacists can leverage their expertise to counsel patients on dietary changes, hydration strategies, and the implications of over-the-counter medications that may affect renal function.
3. **Collaborative Patient Care:** Pharmacists frequently collaborate with physicians and other healthcare providers to optimize treatment regimens for patients with kidney disease. Integrating pharmacists into healthcare teams ensures a more holistic approach, where medication regimens are put into context with renal function assessments, enhancing overall patient safety and efficacy [24].
4. **Monitoring and Follow-Up:** Vigilant monitoring of patients' renal function is essential, especially for those on high-risk medications. Pharmacists can establish follow-up protocols, reviewing laboratory values, identifying trends in renal function, and intervening as necessary to prevent complications.
5. **Research and Quality Improvement:** Pharmacists are increasingly involved in quality improvement projects focusing on renal health. By analyzing data regarding medication-related outcomes in patients with chronic kidney disease (CKD) and participating in research focused on optimizing drug therapy in this population, pharmacists contribute to evolving treatment paradigms [23].

Dosage Adjustment Guidelines for Common Pediatric Medications:

Renal insufficiency in pediatric patients complicates the management of various medical conditions, necessitating particular caution in the prescription of medications. The kidneys play an essential role in the metabolism and excretion of many drugs, and when their function is compromised, the pharmacokinetics of these medications can be significantly affected. Consequently, dosage adjustments become necessary to reduce the risk of toxicity while ensuring therapeutic efficacy [25].

Renal insufficiency, characterized by the inability of the kidneys to adequately filter waste and maintain fluid and electrolyte balance, can be acute or chronic. In children, causes of renal insufficiency can range from congenital anomalies, infections, and genetic conditions to systemic diseases, such as diabetes or hypertension. Given the immature renal function in neonates and young children, dosage adjustments often differ significantly from those in adults. Pediatricians need to be cognizant of this variability due to the dynamic changes in renal function that accompany growth and development [25].

Pharmacokinetics encompasses the absorption, distribution, metabolism, and excretion of drugs, with renal function primarily influencing the latter two processes. Medications can exhibit altered bioavailability and half-lives in patients with impaired renal function. For instance, decreased glomerular filtration rate (GFR) can lead to drug accumulation, increasing the risk of adverse effects. By understanding how renal insufficiency modifies these pharmacokinetic parameters, clinicians can tailor medication regimens accordingly.

The process of adjusting drug dosages in pediatric patients with renal insufficiency involves careful consideration of several factors: the degree of renal impairment, specific drug characteristics, and the clinical condition being treated. The two most widely used methods for assessing renal function in pediatrics are serum creatinine levels and urinary output, with the Schwartz formula often used to estimate GFR [26].

1. **Mild Renal Impairment:** In cases where GFR is mildly decreased (more than 50% of normal), it is generally safe to continue standard dosing but monitor closely for efficacy and toxicity.

2. **Moderate Renal Impairment:** When GFR is between 30-50 mL/min, dose modifications may be necessary. This might include reducing the frequency of dosing or lowering the dose to avoid drug accumulation.
3. **Severe Renal Impairment:** For GFR below 30 mL/min, substantial dose reductions and increased monitoring are critical. In some instances, an alternative medication that does not rely heavily on renal excretion may be preferable. Intermittent hemodialysis can also necessitate adjustments [27].

Common Pediatric Medications and Dosage Adjustments

Several common medications typically require dosage adjustments when utilized in pediatric patients with renal insufficiency. Below are some examples:

1. Antibiotics

- **Gentamicin and Tobramycin:** Aminoglycosides are primarily renally excreted, and their nephrotoxicity necessitates careful monitoring of serum levels. In moderate impairment (GFR of 30-50 mL/min), dosing might be adjusted to every 36-48 hours rather than the standard dosing interval.
- **Penicillins (e.g., Amoxicillin):** While amoxicillin generally requires minimal adjustment in mild renal insufficiency, moderate insufficiency may necessitate a reduction in the dose from 40 mg/kg to 20 mg/kg, administered every 12 hours [28].

2. Antiviral Medications

- **Acyclovir:** In pediatric patients, acyclovir clearance is significantly affected by renal function. Standard dosing (10-15 mg/kg) needs adjustment in cases of moderate to severe renal insufficiency — often halved and monitored for renal function.

3. Analgesics and Antipyretics

- **Ibuprofen:** As an NSAID, ibuprofen is contraindicated in acute renal failure. In chronic renal insufficiency (GFR < 50 mL/min), it is advisable to switch to acetaminophen, where appropriate, and monitor for toxicity closely.

4. Antiepileptic Drugs

- **Levetiracetam:** This drug is primarily eliminated by the kidneys. In mild renal impairment, a dose reduction of 50% is generally recommended, with further adjustments depending on GFR and patient response [29].

Considerations for Maximum Efficacy and Safety

Clinicians must engage in a multi-faceted approach to ensure safety and efficacy when prescribing medications to pediatric patients with renal insufficiency. This involves not only understanding pharmacokinetic adjustments but also remaining vigilant about potential side effects and therapeutic monitoring.

It is essential for healthcare providers to maintain an ongoing dialogue with the family, advocating for careful dietary management and fluid balance to support renal function. Regular follow-up visits should focus on assessing renal function and adjusting medication regimens as necessary [30].

Monitoring and Managing Adverse Drug Reactions:

Adverse drug reactions (ADRs) represent a significant public health concern, contributing to increased morbidity, prolonged hospital stays, and elevated healthcare costs. In many instances, ADRs can result in serious complications or even death. Consequently, the monitoring and management of these reactions is critical in optimizing patient safety and therapeutic efficacy. Pharmacists, as medication experts, play a pivotal role in this endeavor [31].

Understanding Adverse Drug Reactions

ADRs encompass any noxious and unintended response to a drug administered at a normal dosage for the prophylaxis, diagnosis, or treatment of a disease, or for the modification of physiological function. These reactions can be classified into two

main categories: Type A and Type B reactions. Type A reactions, also known as predictable reactions, are dose-dependent and often directly related to the pharmacological effect of the drug. Examples include sedation from antihistamines or bleeding from anticoagulants. On the other hand, Type B reactions are idiosyncratic and are not predictable based on the pharmacological actions of the drugs. These include allergic reactions, drug interactions that lead to unexpected side effects, or toxic effects resulting from metabolic abnormalities [32].

The incidence of ADRs can be alarming. Studies suggest that ADRs account for approximately 5-10% of hospital admissions, with an estimated 10-20% of all hospitalized patients experiencing some form of ADR during their stay. The elderly and those with comorbidities are particularly vulnerable to ADRs due to polypharmacy and alterations in pharmacokinetics and pharmacodynamics [33].

The Pharmacist's Role in Monitoring ADRs

Pharmacists are uniquely positioned to monitor and manage ADRs effectively. Their extensive training in pharmacotherapy equips them with the knowledge required to understand the mechanisms, effects, and interactions of medications. This expertise allows pharmacists to identify potential ADRs and take proactive measures to mitigate risks [34].

1. Patient Counseling and Education

One of the primary roles of the pharmacist is to ensure that patients are well informed about their medications. This includes education on how to take medications, potential side effects, and the importance of adhering to prescribed therapies. By providing thorough patient counseling, pharmacists help patients recognize signs of ADRs early, facilitating prompt medical attention. Furthermore, educating patients about the importance of medication adherence can reduce the likelihood of ADRs related to incomplete or incorrect use of medications [35].

2. Monitoring Drug Therapy

Pharmacists conduct medication reviews and reconciliations routinely, particularly during transitions of care. During these reviews, they assess the appropriateness of drug therapy in light of the patient's clinical status and medical history. They also help identify any potential drug-drug interactions or contraindications that could lead to ADRs. Through continuous monitoring,

pharmacists can intervene before ADRs manifest, adjusting dosages, switching medications, or recommending alternative therapies as necessary [36].

3. Adverse Drug Reaction Reporting

Pharmacists are crucial players in the pharmacovigilance systems responsible for the detection and reporting of ADRs. In most healthcare settings, pharmacists are directly involved in collecting data on adverse events and filing reports with regulatory bodies such as the Food and Drug Administration (FDA) or the European Medicines Agency. This reporting is essential for updating safety profiles of drugs, influencing clinical practice guidelines and standards, and informing future prescribing practices [37].

4. Medication Therapy Management (MTM)

Pharmacists actively participate in Medication Therapy Management (MTM) programs, especially in outpatient settings. These programs involve comprehensive assessments of a patient's complete medication regimen to optimize therapeutic outcomes and reduce the risk of ADRs. This practice includes evaluating the efficacy, safety, and appropriateness of each medication, making recommendations to healthcare providers, and routinely following up with patients [38].

Inter-professional Collaboration

The management of ADRs transcends individual responsibilities, necessitating collaborative efforts among healthcare professionals. Pharmacists often work closely with physicians, nurses, and other members of the healthcare team to ensure a comprehensive approach to patient safety. This collaboration is particularly critical in hospital settings, where pharmacists conduct rounds with medical teams to review medication orders and assess patients in real time [39].

Effective communication among healthcare providers is key. Pharmacists can bring attention to potential ADRs detected during their medication reviews, contributing valuable insights into patient care plans. Integrating pharmacists into healthcare teams can lead to better patient outcomes, as evidenced by numerous studies highlighting reduced medication-related errors and decreased hospital readmission rates due to more vigilant monitoring of medications [40].

Collaboration with Healthcare Teams for Optimal Patient Outcomes:

Pediatric renal failure is a complex medical condition that poses significant challenges to healthcare providers, families, and the affected children themselves. The kidneys play a crucial role in maintaining the body's fluid and electrolyte balance, filtering waste products, and ensuring overall metabolic function. When renal function declines or fails in children, it can lead to serious health complications and affect their growth, development, and quality of life. Therefore, a collaborative approach involving a multidisciplinary health care team is essential in the management of pediatric renal failure [41].

Pediatric renal failure can be classified into two main categories: acute renal failure (ARF) and chronic kidney disease (CKD). ARF can develop suddenly due to various factors, such as congenital abnormalities, severe infections, dehydration, or exposure to nephrotoxic agents. In contrast, CKD is characterized by the progressive loss of kidney function over months or years and can result from conditions such as glomerulonephritis, hereditary disorders, or diabetes. Irrespective of the type of renal failure, early diagnosis and intervention are vital to mitigating long-term complications, including end-stage renal disease (ESRD) which may necessitate dialysis or kidney transplantation [42].

The Role of Collaborative Care

Collaboration among health care teams is paramount in the management of pediatric renal failure. A comprehensive approach includes pediatric nephrologists, nurses, dietitians, social workers, pharmacists, and mental health professionals who each contribute their expertise to improve patient outcomes. Here are several core elements that underscore the importance of teamwork in managing pediatric renal failure patients:

1. Integrated Patient Care

A collaborative health care team allows for integrated patient care, ensuring that all aspects of a patient's health are considered. Pediatric nephrologists lead the clinical management of renal conditions, but they rely on nurses to monitor vital signs, administer medications, and assess fluid balance. Dietitians provide critical nutritional counseling that is tailored to the specific requirements of renal patients—balancing

electrolyte intake and ensuring adequate caloric intake for growth and development. Social workers facilitate access to resources like transportation and financial assistance, while mental health professionals address the emotional and psychological challenges faced by both the patient and their family [43].

2. Communication and Coordination

Effective communication is essential for delivering high-quality care. Regular case discussions and interdisciplinary meetings provide a platform for health care professionals to exchange insights on treatment plans, address concerns, and update each other on patient progress. Digital health records can enhance coordination, enabling team members to access real-time information about medication adherence, lab results, and clinical assessments, which ultimately contributes to safer, more effective care [44].

3. Family-Centered Care

Collaboration extends beyond healthcare professionals to include the patient's family as an integral part of the care team. Family engagement is crucial in pediatric care, especially in managing chronic conditions like renal failure. Families need to understand the condition, treatment options, and lifestyle modifications required. Health care teams should communicate with compassion and clarity, encouraging questions and involving family members in shared decision-making processes. Educating families about renal failure empowers them to be active participants in their child's care, enhancing compliance and overall satisfaction with treatment [45].

4. Addressing Psychosocial Factors

Pediatric renal failure significantly affects a child's emotional and social well-being. Children may experience feelings of anxiety, depression, or isolation due to their medical condition and treatment regimen. Health care teams must be attuned to these psychosocial factors and incorporate mental health support into care plans. Collaborative approaches that involve psychologists or child psychiatrists can help children and families develop coping strategies, address behavioral concerns, and foster resilience. A holistic approach to health care recognizes the importance of mental well-being in achieving positive medical outcomes [46].

Evidence-Based Practices

The use of evidence-based practices in the management of pediatric renal failure is vital to achieving the best results. Collaborative care teams can stay updated with the latest clinical guidelines, research findings, and best practices to inform their decision-making. For example, a pediatric nephrologist may emphasize the importance of regular monitoring of kidney function and electrolytes, using established protocols to maintain optimal control of hypertension and prevent complications like hyperkalemia. Collaborative discussions can dissect current evidence on the timing of dialysis initiation, transplant eligibility, and medication regimens, ensuring that every patient receives personalized care tailored to their unique circumstances [47].

Despite the benefits of collaborative care, several challenges can impact effectiveness. Resistance to interdisciplinary collaboration may arise from professional silos, communication gaps, or institutional barriers. To promote cooperation among team members, health care institutions should cultivate a culture of collaboration through training programs, team-building exercises, and fostering mutual respect. Utilizing technology, such as shared electronic health records and communication platforms, can bridge gaps and enhance cooperation [48].

Ongoing professional development is equally important. Continuing education programs focusing on interdisciplinary practice can increase awareness of the collaborative roles played by different healthcare professionals, fostering appreciation for diverse skill sets. Organizations can host workshops, simulations, or seminars that encourage team-based learning and promote a shared mission of improving pediatric renal care [49].

Future Directions and Challenges in Pediatric Pharmacotherapy:

The management of children with renal impairment poses unique challenges that necessitate an integrated and adaptive approach. Renal impairment, which refers to the decreased ability of the kidneys to filter waste and excess substances from the blood, can lead to significant morbidity. In pediatric populations, the treatment landscape for renal impairment is evolving, characterized by emerging therapeutic options, technological advancements, and a growing emphasis on personalized medicine [50].

Renal impairment in children can arise from various congenital or acquired conditions, including congenital anomalies of the kidney and urinary tract (CAKUT), glomerulonephritis, and systemic diseases such as diabetes mellitus. The prevalence of chronic kidney disease (CKD) among children is estimated to be around 1 in 1,000, which represents a significant health concern. CKD can lead to several complications that necessitate careful management. Children with renal impairment often require ongoing medication management to control blood pressure, manage electrolyte imbalances, and treat underlying conditions. However, their unique physiology and developmental considerations require a careful and often different approach compared to adults [51].

Future Trends in Drug Treatment

1. **Precision Medicine:**
One of the most promising directions for drug treatment in pediatric renal impairment is precision medicine. Advances in genetic research are enabling healthcare providers to tailor treatments based on the individual genetic makeup of patients. For example, pharmacogenomic testing can help determine the most effective and least harmful medications for children with renal impairment, taking into account how their bodies metabolize drugs. This tailored approach can optimize therapeutic outcomes and minimize adverse effects [52].
2. **Novel Therapeutics:**
The pharmaceutical industry is increasingly investing in the development of novel therapies aimed specifically at pediatric populations. With an emphasis on clinical trials that include children, there are potential breakthroughs on the horizon, ranging from biologics to gene therapies that target the underlying mechanisms of renal diseases. For instance, advancements in monoclonal antibody therapies could provide new avenues of treatment for glomerular diseases, thus improving renal preservation and overall health outcomes for affected children [52].
3. **Device Technology and Drug Delivery Systems:**
Innovations in drug delivery systems are expected to transform how medications are

administered to children with renal impairment. Developments in wearable technology and smart inhalers that integrate medication with electronic monitoring could enhance adherence to treatment regimens. Similarly, implantable devices that release medications gradually could better manage chronic conditions without the need for frequent dosing. This integration of technology could facilitate better control of fluid balance and electrolyte levels [53].

4. **Telemedicine:**
The COVID-19 pandemic has accelerated the adoption of telemedicine, a trend likely to persist in managing pediatric renal impairment. Remote consultations can provide timely access to healthcare providers, especially in rural or underserved areas. This can enable ongoing monitoring of renal function and adjustment of medication regimens without necessitating frequent travel to clinics or hospitals, thereby improving adherence and outcomes.
5. **Focus on Supportive Care:**
Future drug treatments are expected to extend beyond pharmacologic interventions. There is growing recognition of the importance of supportive care, including nutritional interventions and psychological support, in managing the health of children with renal impairment. Addressing these holistic aspects can significantly improve quality of life and treatment adherence [54].

Challenges in Drug Treatment for Children with Renal Impairment

While the trends detailed above offer a promising outlook, several challenges remain in the field of pediatric nephrology:

1. **Drug Safety and Efficacy:**
One of the primary challenges in drug treatment for children is the lack of robust clinical trials specifically involving pediatric populations. Many medications used in pediatric nephrology are prescribed based on adult studies, which can lead to uncertainties regarding appropriate dosages and potential side effects in children. The underrepresentation of children in clinical

research raises concerns about the safety and efficacy of treatments that are often extrapolated from adult data [55].

2. Renal Physiology Variability:

The pharmacokinetics of drugs can significantly differ in children with renal impairment compared to adults. The immature renal function in infants and toddlers, along with developmental changes in older children, complicates medication dosing. Therefore, healthcare providers must have a profound understanding of these differences to avoid overdosing or underdosing pediatric patients [56].

3. Complexity of Comorbid Conditions:

Children with renal impairment often have coexisting health issues, including cardiovascular problems, obesity, and diabetes, necessitating polypharmacy. Managing multiple medications raises the risk of drug-drug interactions, complicating treatment regimens. Clinicians must carefully balance various therapeutic needs while ensuring that overall treatment goals align with the child's health status and family circumstances.

4. Access to Care:

Socioeconomic factors play a crucial role in treatment accessibility. Children with renal impairment may face barriers to receiving optimal care, including financial constraints, geographical limitations, and variations in health insurance coverage. Disparities in access to specialized nephrology services can lead to unequal health outcomes among children, exacerbating existing inequalities in health care [57].

5. Parental Education and Involvement:

The success of drug treatment hinges not only on medical interventions but also on the active involvement of parents and guardians in managing their child's condition. However, achieving meaningful parental engagement can be challenging, especially when families face educational or language barriers. Comprehensive educational programs tailored to the specific needs of children with renal impairment can empower families to make informed decisions about treatment [58].

Conclusion:

In conclusion, the role of pharmacists in managing pediatric dosage adjustments for renal impairment is

essential to ensuring safe and effective medication therapy for vulnerable populations. Pharmacists bring specialized knowledge of pharmacokinetics and pharmacodynamics, enabling them to make critical decisions regarding drug dosing based on a child's unique renal function. Their expertise not only facilitates appropriate dosage modifications but also enhances patient safety through vigilant monitoring of drug effects and potential adverse reactions. By collaborating with healthcare teams and educating caregivers, pharmacists contribute significantly to developing individualized treatment plans that optimize therapeutic outcomes while minimizing risks. As pediatric patients with renal impairment continue to present unique challenges, ongoing research and training in this area will be vital in further enhancing the pharmacist's role in promoting safe medication practices and improving the overall quality of care in pediatric nephrology.

References:

1. Malik L, Mejia A, Weitman S. Eligibility of patients with renal impairment for Phase I trials: time for a rethink? *Eur J Cancer*. 2014;50(17):2893–2896.
2. Becherucci F, Roperto RM, Materassi M, Romagnani P. Chronic kidney disease in children. *Clin Kidney J*. 2016;9(4):583–591.
3. Schwartz GJ, Work DF. Measurement and estimation of GFR in children and adolescents. *Clin J Am Soc Nephrol*. 2009;4(11):1832–1843.
4. Rhodin MM, Anderson BJ, Peters AM, et al. Human renal function maturation: a quantitative description using weight and postmenstrual age. *Pediatr Nephrol*. 2009;24(1):67–76.
5. Zhang L, Xu N, Xiao S, et al. Regulatory perspectives on designing pharmacokinetic studies and optimizing labeling recommendations for patients with chronic kidney disease. *J Clin Pharmacol*. 2012;52(1 suppl):79S–90S.
6. Schwartz GJ, Munoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol*. 2009;20(3):629–637.

7. U.S. Department of Health and Human Services. Revised draft guidance for industry on pharmacokinetics in patients with impaired renal function—study design, data analysis, and impact on dosing and labeling; availability. Federal Register. 2010;75(54):13562.
8. Daschner M. Drug dosage in children with reduced renal function. *Pediatr Nephrol*. 2005;20(12):1675–1686.
9. Schwartz GJ, Work DF. Measurement and estimation of GFR in children and adolescents. *Clin J Am Soc Nephrol*. 2009;4(11):1832–1843.
10. Aronoff GR, Bennett WM, Berns JS, et al. Drug Prescribing in Renal Failure: Dosing Guidelines for Adults and Children. 5th ed. Philadelphia, PA: American College of Physicians; 2007.
11. Sage DP, Kulczar C, Roth W, Liu W, Knipp GT. Persistent pharmacokinetic challenges to pediatric drug development. *Front Genet*. 2014;5(281):1–8.
12. Wahba IM, Olyaei AJ, Rozansky D, Bennett WM. Handling of drugs in children with abnormal renal function. In: Avner E, Harmon W, Niaudet P, Yoshikawa N, eds. *Pediatric Nephrology*. Berlin, Heidelberg: Springer-Verlag; 2009: 1693–1711.
13. Zhang Y, Mehta N, Muhari-Stark E, Burckart GJ, Van Den Anker J, Wang J. Pediatric renal ontogeny and applications in drug development. *J Clin Pharmacol*. 2019;59(suppl 1):S9–S20.
14. Spadoni C. Pediatric drug development: Challenges and opportunities. *Curr Ther Res Clin Exp*. 2019;90:119–122.
15. Group KKDIGOCW. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3(1):1–150.
16. Miscellaneous. Chapter 6: CKD among children and adolescents. *Am J Kidney Dis*. 2019;73(3 suppl 1):S125–S132.
17. Miscellaneous. Chapter 7: ESRD among children, adolescents, and young adults. *Am J Kidney Dis*. 2018;71(3 Suppl 1):S383–S416.
18. Lea-Henry TN, Carland JE, Stocker SL, Sevastos J, Roberts DM. Clinical pharmacokinetics in kidney disease: fundamental principles. *Clin J Am Soc Nephrol*. 2018;13(7):1085–1095.
19. Rao S, Abzug MJ, Carosone-Link P, et al. Intravenous acyclovir and renal dysfunction in children: a matched case control study. *J Pediatr*. 2015;166(6):1462 e1–1468 e4.
20. Shirkey H. Therapeutic orphans. *J Pediatr*. 1968;72(1):119–120.
21. Alshammari, S. A., Alshammari, A. S., Alshammari, H. S., & Ahamed, S. S. (2023). Overview of hypertension in Saudi Arabia: A systematic review and meta-analysis. *Saudi Medical Journal*, 44(10), 951–964.
22. Fink, J. C., & Chertow, G. M. (2009). Medication errors in chronic kidney disease: One piece in the patient safety puzzle. *Kidney International*, 76(11), 1123–1125.
23. Bikbov, B., Purcell, C. A., Levey, A. S., Smith, M., Abdoli, A., Abebe, M., Adebayo, O. M., Afarideh, M., Agarwal, S. K., & Agudelo-Botero, M. (2020). Global, regional, and national burden of chronic kidney disease, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. *The Lancet*, 395(10225), 709–733.
24. Al-Abdelmuhsin, L., Al-Ammari, M., Babelghaith, S. D., Wajid, S., Alwhaibi, A., Alghadeer, S. M., Al Arifi, M. N., & Alrabiah, Z. (2021). Assessment of pharmacists' knowledge and practices towards prescribed medications for dialysis patients at a tertiary hospital in Riyadh Saudi Arabia. *Healthcare*, 9(9), 1098.
25. Daniel, W. W. (1978). *Biostatistics: A foundation for analysis in the health sciences*. Wiley.
26. Alqahtani, B., Elnaggar, R. K., Alshehri, M. M., Khunti, K., & Alenazi, A. (2023). National and regional prevalence rates of diabetes in Saudi Arabia: Analysis of national survey data. *International Journal of Diabetes in Developing Countries*, 43(3), 392–397.
27. Alobaidi, S. (2021). Knowledge of chronic kidney disease among the population of Saudi Arabia evaluated using a validated questionnaire: A cross-sectional study. *Patient Preference and Adherence*, 15, 1281–1288.
28. Drenth-van Maanen, A. C., van Marum, R. J., Jansen, P. A. F., Zwart, J. E. F., van Solinge, W. W., & Egberts, T. C. G. (2015). Adherence

- with dosing guideline in patients with impaired renal function at hospital discharge. *PLoS One*, 10(6), e0128237.
29. Al-Abdelmuhsin, L., Al-Ammari, M., D Babelghaith, S., Wajid, S., Asiri, Y. A., Almetawazi, M. S., Alghadeer, S. M., & Al-Arifi, M. N. (2020). Pharmacist-led medication counseling for patients undergoing hemodialysis: A path to better adherence. *International Journal of Environmental Research and Public Health*, 17(7), 2399.
 30. Alzahrani, N. S., Almarwani, A. M., Alhowaymel, F., & Alharbi, H. F. (2023). The lived experience of middle-aged Saudi patients with end-stage chronic renal disease on hemodialysis treatment. *Journal of Transcultural Nursing*, 34(4), 263–269.
 31. Banerjee, D., Winocour, P., Chowdhury, T. A., De, P., Wahba, M., Montero, R., Fogarty, D., Frankel, A. H., Karalliedde, J., Mark, P. B., Patel, D. C., Pokrajac, A., Sharif, A., Zac-Varghese, S., Bain, S., Dasgupta, I., On behalf of the Association of British Clinical, D., & The Renal, A. (2022). Management of hypertension and renin-angiotensin-aldosterone system blockade in adults with diabetic kidney disease: Association of British Clinical Diabetologists and the Renal Association UK guideline update 2021. *BMC Nephrology*, 23(1), 9.
 32. Callis L, Vila A, Catala J, Gras X. Long-term treatment with captopril in pediatric patients with severe hypertension and chronic renal failure. *Clin Exp Hypertens A*. 1986;8(4–5):847–851.
 33. Al-Mayouf SM, Alameer A, Alfattani A, Alsonbul A. Outcome of childhood lupus nephritis in Saudi children. *Saudi J Kidney Dis Transpl*. 2017;28(5):1015–1020.
 34. McMahon KR, Harel-Sterling M, Pizzi M, Huynh L, Hessey E, Zappitelli M. Long-term renal follow-up of children treated with cisplatin, carboplatin, or ifosfamide: a pilot study. *Pediatr Nephrol*. 2018;33(12):2311–2320.
 35. Ouellet D, Bockbrader HN, Wesche DL, Shapiro DY, Garofalo E. Population pharmacokinetics of gabapentin in infants and children. *Epilepsy Res*. 2001;47(3):229–241.
 36. Stitt G, Morris J, Schmees L, Angelo J, Akcan Arian A. Cefepime pharmacokinetics in critically ill pediatric patients receiving continuous renal replacement therapy. *Antimicrob Agents Chemother*. 2019;63(4):e02006.
 37. Soltani M, Tobin CM, Bowker KE, Sunderland J, Macgowan AP, Lovering AM. Evidence of excessive concentrations of 5-flucytosine in children aged below 12 years: a 12-year review of serum concentrations from a UK clinical assay reference laboratory. *Int J Antimicrob Agents*. 2006;28(6):574–577.
 38. Tedeschi S, Tumietto F, Conti M, Giannella M, Viale P, Team SOaS. Use of daptomycin in critically ill children with bloodstream infections and complicated skin and soft-tissue infections. *Pediatr Infect Dis J*. 2016;35(2):180–182.
 39. Murry DJ, Sandlund JT, Stricklin LM, Rodman JH. Pharmacokinetics and acute renal effects of continuously infused carboplatin. *Clin Pharmacol Ther*. 1993;54(4):374–380.
 40. Bajee IA, Khatri S, Tresa V, Hashmi S, Mubarak M, Lanewala AA. Histopathological spectrum and short-term outcome of treatment with cyclophosphamide in relapsing steroid-sensitive nephrotic syndrome. *J Coll Physicians Surg Pak*. 2018;28(6):436–439.
 41. Florescu DF, Chambers HE, Qiu F, et al. Cidofovir in pediatric solid organ transplant recipients: University of Nebraska experience. *Pediatr Infect Dis J*. 2015;34(1):47–51.
 42. Halkin H, Radomsky M, Millman P, Almog S, Blieden L, Boichis H. Steady state serum concentrations and renal clearance of digoxin in neonates, infants and children. *Eur J Clin Pharmacol*. 1978;13(2):113–117.
 43. Watt KM, Avant D, Sherwin J, et al. Effect of renal function on antihypertensive drug safety and efficacy in children. *Pediatr Nephrol*. 2018;33(1):139–146.
 44. Yusuf U, Hale GA, Carr J, et al. Cidofovir for the treatment of adenoviral infection in pediatric hematopoietic stem cell transplant patients. *Transplantation*. 2006;81(10):1398–1404.
 45. Rusconi F, Assael BM, Boccazzi A, et al. Aztreonam in the treatment of severe urinary tract infections in pediatric patients. *Antimicrob Agents Chemother*. 1986;30(2):310–314.
 46. Lowis SP, Pearson AD, Newell DR, Cole M. Etoposide pharmacokinetics in children: the development and prospective validation of a

-
- dosing equation. *Cancer Res.* 1993;53(20):4881–4889.
47. Hodges UM, Berg S, Naik SK, Bower S, Lloyd-Thomas A, Elliot M. Filtration of fentanyl is not the cause of the elevation of arterial blood pressure associated with post-bypass ultrafiltration in children. *J Cardiothorac Vasc Anesth.* 1994;8(6):653–657.
 48. Wong SF, Leung MP, Chan MY. Pharmacokinetics of fluconazole in children requiring peritoneal dialysis. *Clin Ther.* 1997;19(5):1039–1047.
 49. Kohagura, K. (2023). The public health impact of hypertension and diabetes: A powerful tag team for the development of chronic kidney disease. *Hypertension Research*, 46(2), 339–340.
 50. Hassanien, A. A., Al-Shaikh, F., Vamos, E. P., Yadegarfar, G., & Majeed, A. (2012). Epidemiology of end-stage renal disease in the countries of the Gulf Cooperation Council: A systematic review. *JRSM Short Reports*, 3(6), 1–21.
 51. Teh, X. R., & Lee, S. W. H. (2019). Pharmacists' attitude, self-reported knowledge and practice of dosage adjustment among chronic kidney disease patients in Malaysia. *Journal of Pharmacy Practice and Research*, 49(2), 179–185.
 52. Joy, M. S., DeHart, R. M., Gilmartin, C., Hachey, D. M., Hudson, J. Q., Pruchnicki, M., Dumo, P., Grabe, D. W., Saseen, J., & Zillich, A. J. (2005). Clinical pharmacists as multidisciplinary health care providers in the management of CKD: A joint opinion by the nephrology and ambulatory care practice and research networks of the American college of clinical pharmacy. *American Journal of Kidney Diseases*, 45(6), 1105–1118.
 53. Kearney, P. M., Whelton, M., Reynolds, K., Muntner, P., Whelton, P. K., & He, J. (2005). Global burden of hypertension: Analysis of worldwide data. *The Lancet*, 365(9455), 217–223.
 54. Wallace, K. L., Beckett, R. D., & Sheehan, A. H. (2014). Pharmacist perception and use of UpToDate®. *Journal of the Medical Library Association : JMLA*, 102(4), 296–300.
 55. Saleem, A., Masood, I., & Khan, T. M. (2017). Clinical relevancy and determinants of potential drug-drug interactions in chronic kidney disease patients: Results from a retrospective analysis. *Integrated Pharmacy Research & Practice*, 6, 71–77.
 56. Ginawi, I. A., Ahmed, H. G., & Al-Hazimi, A. M. (2014). Assessment of risk factors for chronic kidney disease in Saudi Arabia. *International Journal of Science and Research*, 3, 446–450.
 57. Kaneyama, A., Hirata, A., Hirata, T., Imai, Y., Kuwabara, K., Funamoto, M., Sugiyama, D., & Okamura, T. (2023). Impact of hypertension and diabetes on the onset of chronic kidney disease in a general Japanese population. *Hypertension Research*, 46(2), 311–320.
 58. Santos-Díaz, G., Pérez-Pico, A. M., Suárez-Santisteban, MÁ, García-Bernalt, V., Mayordomo, R., & Dorado, P. (2020). Prevalence of potential drug–drug interaction risk among chronic kidney disease patients in a Spanish hospital. *Pharmaceutics*, 12(8), 713.