NEAR EAST UNIVERSITY
INSTITUTE OF GRADUATE STUDIES
DEPARTMENT OF CLINICAL PHARMACY

ASSESMENT OF POTENTIAL DRUG-DRUG INTERACTIONS IN THE CARDIOLOGY CLINICS

M.Sc THESIS

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Approval

We certify that we have read the thesis submitted by **BELAL MUSTAFA ABDULWAHAB AL-MUHAYA titled "ASSESMENT OF POTENTIAL DRUG-DRUG INTERACTIONS IN CARDIOLOGY CLINIC"** and that in our combined opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Educational Sciences.

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DECLARATION

I hereby declare that all information, documents, analysis, and results in this thesis have been collected and presented according to the academic rules and ethical guidelines of the Institute of Graduate Studies, Near East University. I also declare that as required by these rules and conduct, I have fully cited and referenced information and data that are not original to this study.

BELAL MUSTAFA ABDULWAHAB ALMUHAYA

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ASSESMENT OF POTENTIAL DRUG-DRUG INTERACTIONS IN THE CARDIOLOGY CLINICS

ABSTRACT

Purpose

This study aimed to assess the prevalence of potential drug-drug interactions among cardiology patients at the Near East University Hospital in Turkish Republic of Northern Cyprus.

Methodology

A retrospective analysis was conducted on eligible patients who were hospitalized in the cardiology clinics at NEUH between December 1st, 2022, and December 1st, 2023. Patients who are older than 17 years old and had more than one medication prescribed were included in the study. Potential drug-drug interactions (pDDIs) were identified using interaction checkers from Drugs.com and Medscape.com. The detected pDDIs were categorized based on their severity.

Results:

The study revealed a high prevalence of pDDIs among cardiology patients, with 80% of patient files showed at least one potential interaction, Drugs.com showed more interaction than Medscape. The was a significant association between the age and interaction ($p<0.05$).

Conclusion:

The study showed a high frequency of pDDIs in cardiology clinic, generally due to commonly used high risk medication prescribed in cardiology clinics. Our findings showed that the number of pDDIs was detected higher using drugs.com compared to Medscape. Due to the retrospective nature of the study, we were unable to determine whether the identified pDDIs were clinically relevant. Therefore, by identifying the most common medications at risk of drug-drug interactions, this study can assist healthcare professionals in recognizing drugs with a higher likelihood of such interactions.

Keywords: DDIs, cardiology patients, Pharmacological approaches, mobile applications, Cyprus

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LIST OF ABBREVIATION

Abbreviation	Full Form
DDIs	Drug-Drug Interactions
HER	Electronic Health Record
ICU	Intensive Care Unit
NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
VTE	Venous Thromboembolism
LMWH	Low-Molecular-Weight Heparin
CAT	Cancer-Associated Thrombosis
ESC	European Society of Cardiology
ISTH	International Society on Thrombosis and Haemostasis
CHEST	American College of Chest Physicians
SSC	Scientific and Standardization Committee

CHAPTER I

INTRODUCTION

This section aims to provide a succinct overview and foundational context regarding potential interactions among medications administered to patients hospitalized at the internal clinic. It encompasses the problem statement, underscores the significance of the study, outlines its objectives and constraints, delineates the research inquiries it aims to resolve, and offers clarification on pertinent terminology.

In the realm of cardiology, where precision and efficacy are paramount, the impact of drug-drug interactions (DDIs) on medication adherence and treatment outcomes has emerged as a critical area of concern. As cardiovascular diseases continue to be a leading cause of morbidity and mortality globally, the intricate interplay between various medications prescribed for these conditions necessitates a thorough understanding of potential interactions. DDIs have the potential to compromise the effectiveness of therapeutic regimens, exacerbate adverse effects, and impede patients' adherence to prescribed medications(Thompson et al., 2023).

Achieving optimal treatment outcomes in cardiology requires not only the prescription of appropriate medications but also a nuanced comprehension of how these drugs may interact with one another. The complexity of cardiovascular conditions often leads to the prescription of multiple medications, each targeting specific aspects of the disease. Consequently, the risk of DDIs escalates, posing a challenge to healthcare professionals in ensuring patient safety and treatment efficacy(Kalash et al., 2023).

This study explores the multifaceted impact of DDIs on medication adherence and treatment outcomes in cardiology patients. It delves into the intricacies of drug interactions specific to cardiovascular medications, shedding light on potential pitfalls that may compromise the effectiveness of therapeutic interventions. Furthermore, the assessment and management strategies aimed at mitigating these interactions are elucidated, emphasizing the need for a comprehensive and patient-centric approach(Li, 2023).

Understanding the significance of DDIs in cardiology is not merely an academic pursuit but a crucial aspect of providing quality healthcare. As we navigate the delicate balance between therapeutic benefits and potential complications, it becomes imperative for healthcare professionals to adopt proactive strategies that optimize medication regimens, enhance

adherence, and ultimately contribute to improved treatment outcomes for cardiology patients. Through a thorough examination of these issues, this paper seeks to contribute valuable insights to the evolving landscape of cardiovascular care, fostering a holistic and informed approach to patient management(Akbar et al., 2021).

Cardiovascular diseases (CVDs) constitute a significant global health challenge, contributing substantially to morbidity and mortality across diverse populations. With an array of pharmacological interventions available, the management of CVD often involves the prescription of multiple medications aimed at addressing various aspects of the disease. As a result, polypharmacy has become a common practice in cardiology, offering a tailored approach to individual patient needs(Nishiuchi et al., 2022).

However, the concomitant use of multiple medications introduces the potential for drug-drug interactions (DDIs), a phenomenon that occurs when the effects of one drug are altered by the presence of another. In the context of cardiology, where precise and consistent medication regimens are crucial for optimal outcomes, DDIs pose a unique challenge. These interactions can range from alterations in drug metabolism and pharmacokinetics to synergistic or antagonistic effects on therapeutic outcomes(Ersoy & Ersoy, 2021).

The pharmacokinetic and pharmacodynamic complexities inherent in cardiovascular medications contribute to the heightened susceptibility to DDIs. Enzyme induction or inhibition altered absorption rates, and variations in drug clearance may lead to unpredictable and sometimes adverse consequences. Moreover, the impact of DDIs extends beyond the pharmacological realm, influencing patient adherence to prescribed regimens(Li, 2023).

Medication adherence, a cornerstone of successful cardiovascular treatment, can be compromised by factors such as complex dosing schedules, adverse effects, and the financial burden associated with multiple medications. The presence of DDIs further amplifies these challenges, potentially leading to suboptimal adherence and, consequently, diminished treatment efficacy(Haleem et al., 2021).

Recognizing the intricate web of interactions that may occur in the pharmacological management of cardiovascular diseases, healthcare professionals are tasked with navigating this complexity to ensure patient safety and positive treatment outcomes. This background underscores the need for a comprehensive understanding of DDIs in cardiology, emphasizing

the critical role that assessment and management strategies play in optimizing therapeutic regimens and enhancing medication adherence(Tiwari & Dwivedi, 2019).

As we delve into the nuanced landscape of DDIs in the context of cardiovascular care, it becomes evident that addressing these challenges requires a multidisciplinary approach. Healthcare providers, pharmacists, and patients must collaborate to implement effective strategies that minimize the risks associated with DDIs, ultimately paving the way for improved patient outcomes in the dynamic field of cardiology(Sheikh-Taha & Asmar, 2021).

Current Challenges in Addressing DDIs in Cardiology

Despite the advancements in cardiovascular pharmacotherapy, addressing drug-drug interactions (DDIs) in cardiology presents a myriad of challenges. The complexity arises from the diversity of cardiovascular conditions, the heterogeneity of patient populations, and the intricate pharmacological profiles of the medications involved. Several key challenges warrant attention:

Multiplicity of medications

Cardiology patients often require a combination of medications targeting various aspects of their condition, such as antiplatelet agents, anticoagulants, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, and diuretics. The increasing number of prescribed medications heightens the likelihood of potential interactions, necessitating a meticulous approach to medication management(Özlek et al., 2019).

In the realm of cardiology, the management of cardiovascular diseases often entails the intricate orchestration of multiple medications. The polypharmacy approach aims to address diverse aspects of the complex pathophysiology associated with various cardiovascular conditions, including hypertension, heart failure, arrhythmias, and atherosclerosis. While this strategy allows for a tailored and comprehensive treatment plan, it simultaneously presents challenges related to the multiplicity of medications(Kamaraju et al., 2021).

Diverse drug classes

Cardiology patients frequently find themselves prescribed medications from various drug classes. Antihypertensives, antiplatelet agents, lipid-lowering drugs, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, diuretics, and anticoagulants are just a few examples of the diverse pharmacological arsenal employed to manage cardiovascular

conditions. Each class of drugs serves a distinct purpose, contributing to the complexity of treatment regimens(Juřica, 2020).

Individualized treatment plans

The heterogeneity of cardiovascular diseases demands individualized treatment plans, often resulting in a unique combination of medications tailored to address a patient's specific condition, risk factors, and comorbidities. This personalized approach enhances therapeutic efficacy but simultaneously elevates the potential for drug-drug interactions (DDIs) due to the intricate interplay of pharmacokinetics and pharmacodynamics (Nusair et al., 2020).

Risk of Polypharmacy-Related Issues

Polypharmacy introduces inherent risks, including increased pill burden, complex dosing schedules, and heightened potential for medication errors. Managing a multitude of medications can be overwhelming for patients, leading to challenges in adherence and understanding the necessity of each prescribed drug. These issues underscore the importance of healthcare providers adopting a patient-centered approach to facilitate effective communication and education (Kovačević et al., 2020).

Impact on Adherence

The multiplicity of medications is a significant determinant of medication adherence in cardiology patients. Complex regimens, coupled with potential side effects, may contribute to non-adherence, jeopardizing treatment efficacy. Adherence challenges are particularly pronounced in chronic conditions, where long-term medication management is imperative to control disease progression and prevent adverse cardiovascular events (Fatunde & Brown, 2020).

Risk of Drug-Drug Interactions (DDIs)

With each added medication, the risk of DDIs escalates. Cardiovascular drugs may interact at various levels, affecting absorption, metabolism, distribution, and elimination. These interactions can lead to altered therapeutic effects, compromised safety, or unexpected adverse events. Vigilance in identifying and managing DDIs is paramount to ensuring the optimal balance between therapeutic benefits and potential risks (Sobrinho et al., 2020).

Continuous medication reassessment

The dynamic nature of cardiovascular diseases necessitates ongoing medication reassessment. Changes in disease status, the emergence of new symptoms, or the development of comorbidities may prompt adjustments to the existing medication regimen. Regular reassessment allows healthcare providers to adapt treatment plans, minimizing unnecessary polypharmacy and optimizing medication combinations (Beavers et al., 2022).

Navigating the multiplicity of medications in cardiology requires a delicate balance between tailoring treatment to individual patient needs and mitigating the associated risks. As the field advances, strategies for simplifying regimens, enhancing patient education, and employing technological solutions will play integral roles in optimizing the management of polypharmacy in cardiovascular care. By addressing these challenges thoughtfully, healthcare professionals can strive to achieve the delicate equilibrium necessary for maximizing treatment benefits while minimizing potential complications associated with the multitude of medications in cardiology (Hammoud & Shapiro, 2022).

Variability in Patient Profiles

Patients with cardiovascular diseases encompass a broad spectrum of demographics, comorbidities, and genetic predispositions. This variability introduces challenges in predicting how individuals may respond to specific drug combinations, making it essential to tailor interventions based on a nuanced understanding of each patient's unique characteristics (Agarwal & Agarwal, 2021).

The landscape of cardiovascular diseases encompasses a diverse array of patients, each presenting with a unique set of characteristics, comorbidities, and genetic predispositions. The variability in patient profiles within the field of cardiology is a multifaceted challenge that demands a personalized and nuanced approach to healthcare delivery. Understanding and navigating this variability is essential for optimizing treatment outcomes and ensuring patient well-being (Mussina et al., 2019).

Demographic diversity

Cardiology patients span a wide range of ages, ethnicities, and socioeconomic backgrounds. Age-related variations in drug metabolism and response to treatment underscore the need for tailored interventions. Additionally, the prevalence of cardiovascular risk factors may differ

among demographic groups, emphasizing the importance of considering individual patient characteristics in treatment decisions (dos Anjos et al., 2019).

Comorbid conditions

Cardiovascular diseases often coexist with various comorbidities, such as diabetes, renal dysfunction, and respiratory conditions. The presence of multiple health issues complicates treatment planning, as medications for cardiovascular management must be carefully selected to avoid exacerbating existing conditions or causing adverse interactions with medications prescribed for comorbidities (Akbulut & Urun, 2020).

Genetic variability

Genetic factors contribute significantly to the variability in patients' responses to cardiovascular medications. Polymorphisms in genes involved in drug metabolism, receptor sensitivity, and drug transporters can influence the pharmacokinetics and pharmacodynamics of medications. Pharmacogenomics considerations are crucial for tailoring treatment plans to individual genetic profiles, optimizing drug efficacy, and minimizing adverse effects (Fatunde & Brown, 2020).

Lifestyle factors

Patient lifestyle choices, including diet, physical activity, and tobacco use, significantly impact cardiovascular health. These lifestyle factors can influence the effectiveness of pharmacological interventions and contribute to the progression or mitigation of cardiovascular diseases. Tailoring treatment plans to accommodate and address these lifestyle factors is essential for comprehensive patient care (Kamaraju et al., 2021).

Psychosocial considerations

The psychosocial aspects of patients' lives, including stress levels, mental health, and social support systems, play a pivotal role in cardiovascular health. Psychological factors can influence adherence to prescribed medications and lifestyle recommendations. Addressing these aspects in a patient-centric manner is crucial for achieving holistic and sustainable improvements in cardiovascular outcomes (Haleem et al., 2021).

Gender-specific Variances

Gender differences in cardiovascular diseases and their response to treatment have been increasingly recognized. Hormonal variations, physiological dissimilarities, and differences in

symptom presentation necessitate gender-specific considerations in cardiovascular care. Tailoring treatment plans to account for these variances is essential for optimizing outcomes in male and female patients (Akbar et al., 2021).

Individual Response to Medications

Each patient's response to medications is inherently unique. While evidence-based guidelines provide a foundation for treatment decisions, healthcare providers must remain vigilant to individual responses, adjusting treatment plans based on ongoing assessment and monitoring. Regular follow-ups allow for the identification of any unexpected reactions or variations in treatment effectiveness (Thompson et al., 2023).

Navigating the variability in patient profiles requires healthcare providers in cardiology to embrace an individualized and patient-centric approach. Tailoring treatment plans based on demographic, genetic, lifestyle, and psychosocial factors is essential for optimizing cardiovascular care and addressing the specific needs of each patient. By acknowledging and adapting to the diverse nature of cardiovascular patients, healthcare professionals can enhance the precision and efficacy of interventions, ultimately improving patient outcomes and quality of life (Li, 2023).

Limited Clinical Evidence

The scarcity of robust clinical trials specifically designed to investigate DDIs in cardiology contributes to a lack of comprehensive evidence-based guidelines. Healthcare professionals often rely on extrapolated data from studies with limited cardiovascular representation, emphasizing the need for targeted research to inform evidence-based decision-making(Ersoy & Ersoy, 2021).

Despite the ever-expanding arsenal of cardiovascular medications, the field faces a persistent challenge: the scarcity of robust clinical evidence specifically tailored to assess drug-drug interactions (DDIs). The dynamic and intricate nature of cardiovascular diseases, coupled with the diverse patient profiles encountered in clinical practice, underscores the critical need for comprehensive and targeted research. Addressing the gaps in clinical evidence is essential to inform evidence-based decision-making and optimize therapeutic outcomes in cardiology (Tiwari & Dwivedi, 2019).

Diversity of Cardiovascular Patients

Cardiovascular patients constitute a heterogeneous population with varying demographics, comorbidities, and genetic predispositions. Limited representation of this diversity in clinical trials hampers the generalizability of findings to real-world scenarios. Tailoring interventions to individual patient profiles requires research that encompasses a broad spectrum of cardiovascular conditions and patient characteristics (Özlek et al., 2019).

Polypharmacy challenges

The multiplicity of medications often prescribed to cardiovascular patients amplifies the complexity of potential interactions. However, clinical trials frequently focus on the safety and efficacy of individual drugs rather than investigating the cumulative impact of polypharmacy. Bridging this gap in evidence is crucial for understanding how combinations of medications commonly used in cardiology may interact and influence treatment outcomes (Juřica, 2020).

Comprehensive assessment of interactions

Current clinical evidence often lacks comprehensive assessments of drug interactions specific to cardiovascular medications. Interactions may extend beyond pharmacokinetic considerations to include pharmacodynamics effects, potentially altering therapeutic outcomes. Research endeavors must encompass a thorough evaluation of the multifaceted aspects of drug interactions to guide clinicians in making informed decisions (Nusair et al., 2020).

Real-world relevance

Clinical trials are conducted under controlled conditions, and patient populations may differ substantially from those encountered in everyday clinical practice. Real-world evidence, derived from observational studies and post-marketing surveillance, is crucial for understanding how cardiovascular medications interact in diverse patient populations and identifying potential interactions that may not be evident in controlled settings (Sheikh-Taha & Asmar, 2021).

Long-term effects and outcomes

Many cardiovascular diseases require long-term management, yet clinical trials often have limited follow-up periods. Understanding the long-term effects of drug interactions, especially in the context of chronic diseases, is essential for guiding clinicians in making sustained and effective treatment decisions that prioritize both safety and efficacy over extended periods (Juřica, 2020).

Special populations

Certain populations, such as the elderly, pregnant women, and those with multiple comorbidities, may be underrepresented or excluded altogether from clinical trials. Tailoring treatment plans to these special populations requires targeted research to assess the unique challenges and interactions that may impact these individuals differently (Fatunde & Brown, 2020).

Addressing the limited clinical evidence in cardiovascular drug interactions necessitates a concerted effort from the research community, pharmaceutical industry, and healthcare providers. Strategies to bridge this gap include:

- Inclusive Trial Designs: Ensuring that clinical trials are designed to include diverse patient populations, considering age, gender, comorbidities, and genetic variability (Sobrinho et al., 2020).

- Real-world Observational Studies: Conducting rigorous observational studies to capture real-world scenarios, patient adherence, and long-term outcomes in diverse populations.

- Pharmacovigilance and Post-marketing Surveillance: Establishing robust pharmacovigilance programs to monitor drug safety in the post-marketing phase, identifying and addressing potential interactions as they emerge in real-world settings (Beavers et al., 2022).

- Collaboration and Data Sharing: Encouraging collaboration among researchers, clinicians, and pharmaceutical companies to share data and insights, fostering a collective effort to advance our understanding of cardiovascular drug interactions (Agarwal & Agarwal, 2021).

By addressing these challenges and enhancing the depth and breadth of clinical evidence, the cardiology community can make informed decisions, improve patient safety, and optimize treatment outcomes in the complex landscape of cardiovascular drug interactions.

Dynamic Nature of Cardiovascular Conditions

The progression and severity of cardiovascular diseases are dynamic, requiring adjustments to treatment regimens over time. As medications are added, modified, or discontinued, the potential for new DDIs or alterations in existing interactions necessitates ongoing vigilance and adaptability in patient management (Mussina et al., 2019).

Ongoing Research and Future Directions

As the landscape of cardiovascular pharmacotherapy evolves, ongoing research plays a pivotal role in enhancing our understanding of drug-drug interactions (DDIs) and refining management strategies. Several avenues of investigation are currently underway to address the complexities associated with DDIs in the context of cardiology (Ersoy & Ersoy, 2021).

Initiating prospective clinical trials specifically designed to assess DDIs in cardiovascular patients is paramount. These trials should encompass diverse patient populations, including those with multiple comorbidities, to provide robust evidence guiding clinical decision-making. The focus should extend beyond isolated drug combinations to evaluate the cumulative effects of polypharmacy in real-world scenarios (Tiwari & Dwivedi, 2019).

Utilizing advanced pharmacokinetic modeling techniques can aid in predicting potential interactions and their consequences. Incorporating individual patient characteristics, such as genetics, age, and renal/hepatic function, into modeling frameworks enhances the precision of predictions. This approach holds promise for tailoring interventions based on a more nuanced understanding of patient-specific factors.

Further exploration of pharmacogenomics markers associated with cardiovascular medications can refine our ability to predict individual responses to specific drugs. Identifying genetic variations that influence drug metabolism and efficacy allows for personalized treatment plans, minimizing the risk of adverse events and optimizing therapeutic outcomes (Özlek et al., 2019).

Harnessing the power of artificial intelligence in analyzing vast datasets can contribute to the identification of subtle patterns and interactions that may go unnoticed through traditional methods. AI algorithms can assist healthcare professionals in predicting potential DDIs, stratifying patient risk, and optimizing medication regimens based on individualized data (Beavers et al., 2022).

Conducting longitudinal studies focusing on patient adherence and its relationship to treatment outcomes is crucial. Understanding the dynamic nature of adherence over time, particularly in the context of evolving treatment plans and changing medications, can inform interventions aimed at sustaining optimal adherence levels (Agarwal & Agarwal, 2021).

Exploring innovative patient-centric approaches, such as digital health interventions and mobile applications, can facilitate continuous monitoring of medication adherence. These

technologies provide opportunities for real-time feedback, educational resources, and personalized support, fostering a proactive patient role in managing their cardiovascular health (Akbulut & Urun, 2020).

In navigating the complex terrain of DDIs in cardiology, future directions should also emphasize the development of practical and user-friendly clinical tools. These tools could assist healthcare professionals in swiftly assessing and managing interactions, ultimately promoting patient safety and treatment efficacy (Beavers et al., 2022).

Prevention and Management of Drug- drug Interactions

Prevention and management of drug-drug interactions (DDIs) are paramount in ensuring patient safety and optimizing therapeutic outcomes in clinical settings. Given the complexity of modern pharmacotherapy, healthcare providers must adopt proactive strategies to mitigate the risks associated with potential interactions between medications.

One of the primary approaches to prevent DDIs is thorough medication reconciliation. This process involves compiling a comprehensive list of all medications that a patient is currently taking, including prescription drugs, over-the-counter medications, supplements, and herbal remedies. By regularly reviewing and updating this list, healthcare providers can identify potential interactions and take appropriate action to minimize risks (Beavers et al., 2022)..

Additionally, healthcare professionals should stay informed about known DDIs through reputable sources such as drug databases, pharmacology textbooks, and clinical practice guidelines. These resources provide valuable information about the pharmacokinetic and pharmacodynamics properties of medications, as well as specific interactions to watch for based on the mechanisms of action of the drugs involved (Agarwal & Agarwal, 2021)..

Another key strategy for preventing DDIs is utilizing electronic prescribing systems and clinical decision support tools. These technologies can alert prescribers to potential interactions in real-time, providing recommendations for alternative medications or dosage adjustments when necessary. By integrating these tools into electronic health records, healthcare providers can streamline the process of identifying and addressing DDIs during prescribing and medication administration.

In cases where DDIs cannot be avoided entirely, effective management strategies are essential. This may include close monitoring of patients for signs and symptoms of adverse effects,

regular follow-up appointments to assess medication efficacy and tolerability, and patient education about potential interactions and how to minimize risks. Additionally, healthcare providers may consider adjusting medication doses, changing the timing of administration, or selecting alternative medications with lower interaction potential.

Collaboration among healthcare professionals is crucial for the effective prevention and management of DDIs. Interdisciplinary teams, including physicians, pharmacists, nurses, and other allied healthcare professionals, can work together to identify, assess, and address potential interactions comprehensively. By leveraging the expertise of each team member and fostering open communication, healthcare organizations can enhance patient safety and optimize medication therapy outcomes (Özlek et al., 2019)..

In conclusion, the prevention and management of drug-drug interactions are essential components of safe and effective medication management. Healthcare providers must employ proactive strategies such as medication reconciliation, staying informed about known interactions, utilizing electronic prescribing systems, and fostering interdisciplinary collaboration to minimize the risks associated with DDIs and ensure the optimal therapeutic outcomes for patients (Akbulut & Urun, 2020)..

Renal Excretion in Cardiology Medications

The process of drug excretion, particularly renal excretion, plays a pivotal role in the pharmacokinetics of many medications used in cardiology. Understanding the dynamics of drug excretion is crucial when exploring the impact of drug-drug interactions (DDIs) on medication adherence and treatment outcomes in cardiology patients. Renal excretion, in particular, influences the clearance of drugs from the body, and alterations in this process due to DDIs can significantly impact therapeutic efficacy and safety (Gorog et al., 2021).

Many medications used in cardiology, including diuretics, ACE inhibitors, and certain antiarrhythmic, undergo renal excretion. The kidneys are responsible for filtering these drugs from the bloodstream and eliminating them from the body. Any disruption in this renal clearance process can lead to the accumulation of drugs, potentially resulting in adverse effects or reduced therapeutic efficacy (Pöss et al., 2012).

Interactions between cardiovascular medications or between cardiovascular drugs and medications used for other conditions can affect renal clearance. Competing for renal

transporters or shared metabolic pathways may lead to altered excretion rates, influencing the overall pharmacokinetics of the drugs involved. Understanding these interactions is essential for predicting and managing potential complications (Raven et al., 2023).

Variability in renal function among patients adds another layer of complexity. Age-related changes, comorbidities such as chronic kidney disease, and genetic factors can influence individual responses to medications undergoing renal excretion. Tailoring treatment plans based on a thorough understanding of these factors is crucial for optimizing drug therapy (Thompson et al., 2023).

Some cardiovascular medications may have inherent nephrotoxic potential, and DDIs can exacerbate this risk. Careful consideration of the cumulative impact of medications on renal function is essential to prevent adverse effects such as acute kidney injury and to promote overall patient safety (Li, 2023).

Regular monitoring of renal function parameters, including serum creatinine and GFR, is essential for identifying any changes that may impact drug excretion. Incorporating these assessments into routine clinical care aids in early detection of potential issues (Akbar et al., 2021).

Healthcare providers should be adept at adjusting medication dosages based on individual renal function and the presence of DDIs. This personalized approach ensures that therapeutic goals are met while minimizing the risk of adverse effects (Nishiuchi et al., 2022).

Empowering patients with knowledge about the importance of maintaining renal health is crucial. Understanding the role of the kidneys in drug elimination and the potential impact of DDIs on renal function fosters a collaborative approach to treatment between healthcare providers and patients (Tiwari & Dwivedi, 2019).

In conclusion, renal excretion is a critical aspect of the pharmacokinetics of many cardiovascular medications. Considering the influence of drug-drug interactions on renal clearance is vital for optimizing treatment outcomes, ensuring medication adherence, and preventing adverse effects in cardiology patients. Integrating these considerations into clinical

practice enhances the precision of cardiovascular care, contributing to improved patient safety and therapeutic efficacy.

Metabolism of Cardiovascular Medications

The metabolism of cardiovascular medications is a complex and dynamic process that significantly influences their pharmacokinetics. Understanding the intricacies of drug metabolism is crucial when exploring the impact of drug-drug interactions (DDIs) on medication adherence and treatment outcomes in cardiology patients. Metabolic pathways, particularly hepatic metabolism, play a pivotal role in determining the bioavailability, efficacy, and safety of cardiovascular drugs (Özlek et al., 2019).

Many cardiovascular medications undergo hepatic metabolism, where enzymes in the liver transform the drugs into metabolites that are either active or inactive. The cytochrome P450 (CYP) enzyme system is a key player in this process, and alterations in its activity can lead to significant DDIs (Kamaraju et al., 2021).

Drug interactions can occur when cardiovascular medications influence the activity of hepatic enzymes. Inhibition of CYP enzymes may lead to increased levels of other co-administered drugs that are substrates for the same enzymes, potentially resulting in toxicity. Conversely, enzyme induction may accelerate the metabolism of certain drugs, reducing their effectiveness (Kovačević et al., 2020).

Genetic variations in hepatic enzymes can contribute to inter-individual variability in drug metabolism. Pharmacogenomics factors may influence the rate at which individuals metabolize specific cardiovascular medications, impacting both treatment response and the potential for DDIs (Beavers et al., 2022).

Changes in metabolism due to DDIs can affect the dosing frequency or require adjustments to the medication regimen. Adherence challenges may arise if patients are prescribed complex regimens or experience alterations in the timing or dosage of their cardiovascular medications (Mussina et al., 2019).

Some cardiovascular medications are administered as prodrugs, which require hepatic metabolism to convert them into their active forms. Understanding the impact of DDIs on the

activation of prodrugs is crucial for predicting treatment efficacy and potential adverse effects (Akbulut & Urun, 2020).

Therapeutic drug monitoring is essential in the context of hepatically metabolized medications. Regular monitoring of drug levels allows healthcare providers to assess the adequacy of dosing, adjust treatment plans as needed, and identify potential interactions affecting drug metabolism (Fatunde & Brown, 2020).

A thorough review of a patient's medication history, including hepatically metabolized cardiovascular drugs, is critical. Identifying potential interactions and understanding the metabolic pathways involved is essential for optimizing therapeutic regimens (Juřica, 2020).

Incorporating pharmacogenomics testing into the assessment of cardiovascular medications aids in identifying genetic variations that may influence drug metabolism. Tailoring treatment plans based on individual genetic profiles enhances the precision of pharmacotherapy (Haleem et al., 2021).

Healthcare providers should use available resources, including drug interaction databases and clinical decision support tools, to screen for potential DDIs. These tools can assist in identifying interactions related to hepatic metabolism and guide informed decision-making.

Educating patients about the importance of medication adherence, especially in the context of changes in dosing frequency or adjustments due to DDIs, is crucial. Clear communication empowers patients to actively participate in their care, contributing to treatment success (Haleem et al., 2021)...

In conclusion, understanding the metabolism of cardiovascular medications, particularly in the context of hepatic metabolism and drug interactions, is pivotal for optimizing treatment outcomes in cardiology. By incorporating these considerations into clinical practice, healthcare providers can navigate the complexities of drug metabolism, enhance medication adherence, and contribute to improved therapeutic efficacy and patient safety.

1.9. Bioavailability in Cardiovascular Medications

The concept of bioavailability, a measure of the fraction of an administered drug that reaches the systemic circulation and is available for therapeutic action, holds profound implications in the realm of cardiovascular medications. Understanding bioavailability becomes paramount

when investigating the impact of drug-drug interactions (DDIs) on medication adherence and treatment outcomes in cardiology patients. Variations in bioavailability influence the efficacy, safety, and overall success of cardiovascular pharmacotherapy (Haleem et al., 2021)..

1. Absorption and Oral Bioavailability:

The oral route is a common mode of administration for cardiovascular medications, and its bioavailability is intricately linked to the drug's absorption from the gastrointestinal tract. DDIs may alter the absorption process, affecting the bioavailability of co-administered drugs and, consequently, their therapeutic effects.

2. Influence of Hepatic First-Pass Metabolism:

Hepatic first-pass metabolism represents a crucial aspect of bioavailability. Cardiovascular drugs metabolized extensively in the liver may experience significant first-pass effects, potentially leading to reduced systemic bioavailability. Interactions affecting hepatic enzymes can modify this process, influencing the bioavailability of co-administered drugs (Mussina et al., 2019)...

3. Variability in Subcutaneous and Intravenous Bioavailability:

Cardiovascular medications administered via alternative routes, such as subcutaneous or intravenous, often have higher bioavailability compared to oral formulations. However, understanding how DDIs may impact the pharmacokinetics of these parenteral formulations is essential for ensuring optimal drug exposure and therapeutic efficacy.

4. Food and Drug Interactions:

Food can influence the absorption of certain cardiovascular medications, impacting bioavailability. DDIs involving interactions with food or nutrients may necessitate adjustments in medication administration, emphasizing the importance of considering dietary factors in the overall management of cardiovascular pharmacotherapy (Haleem et al., 2021)..

5. Impact on Medication Adherence:

Variability in bioavailability may require adjustments to dosing regimens. Patients experiencing changes in the timing or dosage of their cardiovascular medications due to DDIs

may face adherence challenges, underscoring the need for clear communication and patient education.

6. Prodrug Activation and Bioavailability:

Prodrugs, which require enzymatic activation to become therapeutically active, introduce an additional layer of complexity related to bioavailability. DDIs influencing the enzymes responsible for prodrug activation can impact the overall bioavailability of the active drug (Haleem et al., 2021)...

Assessment and Management Strategies:

1. Comprehensive Medication Review:

A comprehensive review of cardiovascular medications, considering their routes of administration and bioavailability, is crucial. Identifying potential DDIs that may affect absorption and subsequent bioavailability guides informed decision-making in treatment planning.

2. Therapeutic Drug Monitoring:

For drugs with narrow therapeutic windows or significant inter-patient variability, therapeutic drug monitoring becomes essential. Regular monitoring allows healthcare providers to assess systemic drug levels, optimize dosing, and manage DDIs impacting bioavailability.

3. Dose Adjustments Based on Bioavailability:

Healthcare providers should be adept at adjusting medication dosages based on changes in bioavailability influenced by DDIs. This personalized approach ensures that therapeutic goals are achieved while minimizing the risk of adverse effects.

Educating patients about the optimal timing of medication administration, especially in relation to meals or other medications, is crucial. Clear communication empowers patients to adhere to prescribed regimens and minimizes the potential impact of DDIs on bioavailability (Mussina et al., 2019)...

In conclusion, the bioavailability of cardiovascular medications is a pivotal factor in achieving therapeutic success. Recognizing how DDIs can influence bioavailability allows healthcare

providers to tailor treatment plans, optimize adherence, and contribute to improved treatment outcomes for cardiology patients. Incorporating these considerations into clinical practice enhances the precision of cardiovascular care, ensuring that the right amount of medication reaches the systemic circulation to exert its intended therapeutic effects.

Distribution Dynamics of Cardiovascular Medications

The process of drug distribution, involving the movement of cardiovascular medications throughout the body, holds paramount significance in the realm of pharmacotherapy. Understanding the intricacies of drug distribution becomes essential when investigating the impact of drug-drug interactions (DDIs) on medication adherence and treatment outcomes in cardiology patients. Variations in drug distribution influence the therapeutic efficacy, safety, and overall success of cardiovascular pharmacotherapy.

Many cardiovascular medications bind to plasma proteins, influencing their distribution and availability at the target site. Drug interactions that affect protein binding may alter the free fraction of medications in the bloodstream, potentially intensifying or diminishing their therapeutic effects.

Cardiovascular medications often target specific organs or tissues. DDIs can influence the distribution of drugs to these target sites, impacting their efficacy. Understanding the tissue-specific distribution of medications aids in predicting and managing interactions that may compromise treatment outcomes.

Some cardiovascular medications may exhibit effects within the central nervous system, requiring penetration of the blood-brain barrier. DDIs that alter drug distribution across this barrier can influence the magnitude and duration of central nervous system effects, potentially leading to therapeutic challenges.

The volume of distribution, a pharmacokinetic parameter representing the apparent space in the body available to contain the drug, influences drug concentrations. DDIs can affect the factors determining distribution volume, potentially leading to altered drug concentrations and variations in therapeutic responses.

Changes in the distribution of cardiovascular medications may necessitate adjustments to dosing regimens. Patients experiencing alterations in the effectiveness or duration of drug

action due to DDIs may face challenges in adhering to prescribed regimens, emphasizing the need for clear communication and patient education.

Prodrugs, which require enzymatic activation to become therapeutically active, introduce considerations related to both metabolism and distribution. DDIs influencing the enzymes responsible for prodrug activation can impact the overall distribution of the active drug within the body.

A comprehensive review of cardiovascular medications, considering their plasma protein binding, tissue-specific effects, and volume of distribution, is essential. Identifying potential DDIs that may influence drug distribution guides informed decision-making in treatment planning.

For drugs with narrow therapeutic windows or significant inter-patient variability, therapeutic drug monitoring becomes essential. Regular monitoring allows healthcare providers to assess drug concentrations, optimize dosing, and manage DDIs impacting drug distribution.

Healthcare providers should be adept at adjusting medication dosages based on changes in distribution characteristics influenced by DDIs. This personalized approach ensures that therapeutic goals are achieved while minimizing the risk of adverse effects.

Educating patients about the potential impact of DDIs on drug distribution and subsequent therapeutic effects is crucial. Clear communication empowers patients to adhere to prescribed regimens, minimizing the potential impact of distribution-related interactions on treatment outcomes.

In conclusion, the distribution dynamics of cardiovascular medications play a pivotal role in achieving therapeutic success. Recognizing how DDIs can influence drug distribution allows healthcare providers to tailor treatment plans, optimize adherence, and contribute to improved treatment outcomes for cardiology patients. Incorporating these considerations into clinical practice enhances the precision of cardiovascular care, ensuring that medications reach their intended targets to exert their therapeutic effects effectively.

The Role of Clinical Pharmacy in Managing Drug-Drug Interactions (DDIs) in Cardiovascular Care

Clinical pharmacy plays a pivotal role in optimizing medication therapy and ensuring patient safety, particularly in the context of managing drug-drug interactions (DDIs) in cardiovascular care. The multifaceted responsibilities of clinical pharmacists encompass various aspects of DDI identification, assessment, management, and education, contributing significantly to the overall quality of patient care.

1. Identification of DDIs:

Clinical pharmacists are adept at reviewing patients' medication profiles and identifying potential interactions. Using their expertise, pharmacists can recognize drugs with known interactions, evaluate the clinical significance of these interactions, and anticipate potential adverse effects or therapeutic challenges.

2. Assessment of Clinical Significance:

Pharmacists play a crucial role in assessing the clinical significance of identified DDIs. They consider factors such as the severity of potential outcomes, the patient's overall health status, and the therapeutic alternatives available. This assessment guides decision-making in collaboration with the healthcare team.

3. Communication with Healthcare Team:

Effective communication is a cornerstone of clinical pharmacy practice. Pharmacists collaborate with physicians, nurses, and other healthcare professionals to discuss identified DDIs, share insights on potential risks or benefits, and collectively determine the most appropriate course of action. This collaborative approach ensures comprehensive patient care.

4. Medication Adjustment and Monitoring:

Clinical pharmacists actively participate in recommending and implementing adjustments to medication regimens to mitigate the impact of DDIs. This may involve dose adjustments, changes in drug formulations, or alterations in the timing of administration. Pharmacists also play a key role in establishing monitoring plans to assess the effectiveness and safety of adjusted regimens.

5. Patient Education and Counseling:

Educating patients about the potential risks and benefits of their medications is integral to clinical pharmacy practice. Pharmacists provide valuable information to patients regarding DDIs, emphasizing the importance of adherence, recognizing and reporting adverse effects, and understanding the rationale behind any changes made to their medication regimens.

Clinical pharmacists leverage technology and decision support systems to enhance their ability to identify and manage DDIs. Electronic health records, clinical decision support software, and pharmacokinetic tools provide valuable resources for pharmacists in assessing interactions, making evidence-based recommendations, and ensuring the safe use of medications.

Clinical pharmacists are increasingly involved in incorporating pharmacogenomic information into their assessments. Understanding how genetic factors influence drug metabolism allows pharmacists to tailor recommendations based on individual patient profiles, reducing the risk of adverse interactions.

Given the dynamic nature of pharmacotherapy and the constant emergence of new medications, clinical pharmacists engage in ongoing education and training. Staying abreast of the latest research, guidelines, and technological advancements ensures that pharmacists are well-equipped to address the evolving landscape of DDIs in cardiovascular care.

Clinical pharmacists actively contribute to research and quality improvement initiatives related to DDIs. They may participate in studies, collaborate on research projects, and implement strategies to enhance the overall understanding and management of interactions in cardiovascular pharmacotherapy.

In summary, the role of clinical pharmacy in managing DDIs in cardiovascular care is multifaceted and indispensable. By leveraging their expertise, collaborating with healthcare teams, employing technology, and prioritizing patient education, clinical pharmacists contribute significantly to the safe and effective use of medications, ultimately enhancing patient outcomes in the complex landscape of cardiovascular pharmacotherapy.

Statement of Problem:

The field of cardiology faces a persistent challenge in managing the impact of drug-drug interactions (DDIs) on treatment outcomes in cardiovascular patients. The complex interplay of multiple medications, each with its own pharmacokinetic and pharmacodynamic properties, poses a significant risk for adverse interactions. Several methods are available to detect interactions between drugs such as mobile applications and databases.

Purpose of Study

The primary objective of this study is to comprehensively assess the drug-drug interactions among cardiology patients. By examining the prevalence, types, and clinical significance of DDIs within this population, the study aims to provide valuable assessment of two different applications.

Significance of the Study:

This study holds significant implications for both clinical practice and patient outcomes in cardiology. Understanding the intricacies of drug-drug interactions in cardiovascular patients is crucial for healthcare providers, allowing them to make informed decisions when designing treatment plans.

CHAPTER II

LITERATURE REVIEW

This chapter presents research-based conceptual definitions, descriptions, and existing literature on the subject matter.

Theoretical Framework

An essential component of treating cardiovascular illnesses is medication adherence, or how closely patients follow their doctors' prescriptions. Patients with cardiovascular diseases frequently need complicated drug regimens to manage arrhythmias, lower cholesterol, regulate blood pressure, and treat other cardiovascular conditions. However, in this patient population, reaching optimal medication adherence presents a significant challenge (Ismail et al., 2018)

The suboptimal adherence seen in cardiology patients is caused by multiple factors. Patients may become overwhelmed by the intricacy of their treatment plans, the necessity of changing their lifestyles, and the existence of concomitant illnesses. In addition, negative consequences, budgetary limitations, inattention, and a lack of awareness regarding the significance of compliance exacerbate the problem. Healthcare professionals must comprehend these difficulties in order to customize solutions that meet the unique requirements of cardiac patients (Akbar et al., 2021)

In cardiology patients, noncompliance with drug regimens is linked to various adverse consequences. Common outcomes include an increase in hospital admissions, a worsening of cardiovascular symptoms, an increase in death rates, and a decline in quality of life. Non-adherence has a significant financial impact as well since it raises the expense of healthcare due to avoidable problems. Understanding the effects of noncompliance highlights the significance of investigating methods to enhance medication compliance in patients with cardiology (Ersoy & Ersoy, 2021)

In order to properly manage their cardiovascular diseases, patients in cardiology frequently take many drugs. Nevertheless, these medications' interactions may result in side effects that jeopardies patient safety and the effectiveness of the treatment. Drug-drug interactions (DDIs) happen when two medications interact to change how one works. This can lead to decreased therapeutic effects or increased toxicity (Kailash et al., 2023)

Drug combinations including beta-blockers, ACE inhibitors, diuretics, and antiplatelet medicines are commonly used in cardiac therapy. As the quantity of prescribed medications climbs, so does the possibility of interactions. Healthcare professionals must be aware of the particular medication combinations frequently used in cardiology in order to properly predict and handle any potential interactions (Sheikh-Taha & Asmar, 2021).

A number of processes, such as pharmacokinetic and pharmacodynamics interactions, can lead to DDIs. Pharmacodynamics interactions influence the way a medicine acts on the body, whereas pharmacokinetic interactions change how a drug is absorbed, distributed, metabolized, or eliminated. Understanding the various kinds of interactions is essential to determining how they might affect cardiac treatment (Patel et al., 2011).

Considering the common use of polypharmacy, the frequency of DDIs in cardiology patients is notable. Healthcare practitioners need to know the frequency of contacts in order to determine the patient population's risk of developing DDIs. Furthermore, understanding the elements raising the chance of interactions can help direct management and preventative tactics (Allabi et al., 2020).

In the management of cardiovascular disorders, achieving favorable treatment results is the ultimate objective. It is essential to comprehend how DDIs and drug adherence affect treatment outcomes in order to maximize cardiac care. The range of treatment outcomes is wide and includes things like better cardiovascular parameters, fewer cardiovascular events, improved quality of life, and general patient satisfaction (Mateti et al., 2011).

In cardiology, medication compliance is closely related to the efficacy of treatment. Patients who take their prescriptions as directed are more likely to reach their goals for lipid profiles, blood pressure, and other cardiovascular benchmarks. The necessity for interventions targeted at enhancing medication-taking behavior is highlighted by the observation that adherence and treatment outcomes are positively correlated (Murtaza et al., 2016).

The existence of DDIs might add unpredictability to treatment results, making it difficult to forecast how well cardiac drugs will work. Drug concentrations may be changed by interactions, which could result in less effective treatment or unanticipated toxicity. In order to maintain optimal efficacy and safety, healthcare practitioners should take into account the potential effects of DDIs while evaluating treatment outcomes and modifying pharmaceutical regimens (Fatunde & Brown, 2020).

In cardiology, a thorough comprehension of treatment outcomes goes beyond clinical measures and takes the patient's general health into account. The comprehensive evaluation of treatment success takes into account psychological factors, lifestyle modification adherence, and quality of life. Healthcare professionals can customize strategies that meet the complex character of cardiovascular care by incorporating these aspects into the evaluation of treatment results (Kovačević et al., 2020).

To sum up, understanding the complex relationships that exist between treatment outcomes, drug-drug interactions, and medication adherence is essential to improving cardiac care. A patient-centered approach in cardiology is enhanced by addressing medication adherence issues, comprehending the importance of DDIs, and thoroughly evaluating treatment outcomes (Özlek et al., 2019). To increase medication adherence, reduce DDIs, and improve overall treatment results for cardiology patients, effective management techniques should include tailored interventions, interdisciplinary teamwork, and continuous patient education.

Related Research

Ensuring medication adherence in cardiology patients is a multifaceted challenge influenced by various factors. Understanding and addressing these factors are crucial for healthcare providers to develop effective interventions that promote adherence and improve overall treatment outcomes (Nusair et al., 2020).

One significant factor contributing to poor medication adherence is the complexity of medication regimens. Cardiology patients often require multiple medications to manage their cardiovascular conditions comprehensively. The sheer number of pills, different dosing schedules, and the need for combination therapies can overwhelm patients, leading to confusion and unintentional non-adherence. Simplifying regimens, providing clear instructions, and employing pill organizers are strategies that can mitigate this complexity-related barrier to adherence (Mussina et al., 2019).

Financial constraints also play a pivotal role in medication adherence. The cost of cardiovascular medications can be a significant burden for many patients, especially those without adequate insurance coverage. High out-of-pocket expenses may lead patients to skip doses, reduce prescribed dosages, or even discontinue medications altogether. Implementing financial assistance programs, exploring generic alternatives, and fostering communication

about cost concerns can help alleviate this barrier and enhance adherence (Agarwal & Agarwal, 2021).

Psychosocial factors, including depression and anxiety, can significantly impact medication adherence in cardiology patients. Mental health conditions may contribute to feelings of hopelessness or apathy, affecting patients' motivation to adhere to their prescribed medications. Identifying and addressing these psychosocial factors through collaborative care involving mental health professionals can positively influence medication adherence (Beavers et al., 2022).

Another crucial aspect is patient education. Limited health literacy and lack of understanding about the importance of medications and their role in managing cardiovascular diseases can hinder adherence. Healthcare providers must engage in clear communication, providing information about the purpose of each medication, potential side effects, and the long-term benefits of adherence. Tailoring educational efforts to the individual patient's comprehension level is essential for fostering a meaningful understanding of their treatment plan (Sobrinho et al., 2020).

Additionally, forgetfulness is a common barrier to medication adherence. Cardiology patients, particularly the elderly, may struggle to remember to take their medications as prescribed. Implementing reminder systems, such as alarms, mobile applications, or pillboxes with designated compartments for each medication, can serve as effective tools to combat forgetfulness and improve adherence (dos Anjos et al., 2019).

Social support and the patient's relationship with healthcare providers also influence adherence. Patients who perceive strong support from family members, friends, and healthcare professionals are more likely to adhere to their medication regimens. Building trust, fostering open communication, and involving family members in the patient's care can contribute to a supportive environment that enhances adherence (Papus et al., 2022).

Cardiology patients often undergo treatment regimens involving multiple medications to address the complexities of cardiovascular conditions. The combination of drugs aims to manage various aspects of cardiac health, including blood pressure regulation, lipid control, and prevention of clot formation. Common drug combinations include beta-blockers with ACE inhibitors, antiplatelet agents combined with statins, and diuretics alongside calcium channel blockers. Recognizing these prevalent combinations is essential for healthcare providers to

anticipate potential interactions and tailor treatment plans to optimize efficacy while minimizing the risk of adverse events (Almazrou & Alaujan, 2022).

Understanding the pharmacological synergy and potential conflicts between drugs in these combinations is crucial. Beta-blockers and calcium channel blockers, for example, may lead to additive effects on heart rate and blood pressure. Conversely, certain combinations may have conflicting actions, such as diuretics potentially reducing the efficacy of ACE inhibitors. Healthcare providers must carefully consider the rationale behind combining specific drugs and actively monitor patients for signs of drug-drug interactions (DDIs) when implementing these common regimens (Ali et al., 2019).

Assessing and identifying drug-drug interactions (DDIs) in cardiology patients require the utilization of various tools and methods. Healthcare providers rely on these resources to ensure patient safety and optimize the efficacy of treatment regimens (Kalash et al., 2023).

Electronic Health Records play a pivotal role in identifying potential DDIs. Integrated clinical decision support systems within EHRs can automatically flag interactions based on the prescribed medications, enabling healthcare providers to assess the risk and make informed decisions. EHRs streamline the process by providing real-time information, enhancing the efficiency of identifying and managing DDIs (Ramos et al., 2018).

Specialized drug interaction databases, such as the Lexicomp, Micromedex, or Epocrates, offer comprehensive information about potential interactions between specific medications. These databases compile data from various sources, including clinical studies, case reports, and pharmacokinetic studies. Healthcare providers can refer to these databases to assess the severity of interactions, mechanisms involved, and recommended management strategies (Berger et al., 2021).

Pharmacogenomics testing involves analyzing an individual's genetic makeup to predict their response to certain medications. While not a direct tool for identifying interactions, pharmacogenomics information can provide insights into how a patient metabolizes specific drugs, aiding in the prediction of potential interactions based on genetic factors. Integrating pharmacogenomics data into patient assessments contributes to a more personalized and targeted approach to managing DDIs (Ismail et al., 2018).

Drug-Drug Interactions (DDIs) represent a complex challenge in clinical medicine, with profound implications for patient safety and treatment efficacy. Clinical pharmacy, as a specialized field within healthcare, plays a pivotal role in deciphering the intricacies of DDIs, particularly concerning drug metabolism, bioavailability, and distribution. This comprehensive exploration delves into the significance of clinical pharmacy in understanding, identifying, and managing DDIs at the molecular and systemic levels (Ali et al., 2019).

The interplay between drugs within the human body is a dynamic process influenced by various factors, and clinical pharmacists are at the forefront of unraveling these complexities. In this discourse, we delve into the critical aspects of drug metabolism, bioavailability, and distribution, elucidating the multifaceted role of clinical pharmacy in mitigating the risks associated with DDIs (Lattard et al., 2023)

Drug metabolism is a pivotal aspect of a drug's journey through the human body, involving enzymatic transformations that impact its pharmacokinetics and therapeutic effects. Clinical pharmacists, armed with their expertise in pharmacology and therapeutics, play a crucial role in understanding and predicting potential DDIs based on the metabolic pathways of drugs.

Clinical pharmacists employ their knowledge of cytochrome P450 enzymes, glucuronidation, and other metabolic pathways to anticipate potential interactions. The catalytic activity of these enzymes can be modulated by various drugs, leading to either inhibition or induction. By scrutinizing drug regimens, clinical pharmacists can identify possible alterations in metabolic pathways, enabling proactive management strategies (Surapat et al., 2021).

Advancements in pharmacogenomics have empowered clinical pharmacists to tailor drug regimens based on individual genetic variations. Understanding a patient's genetic predisposition to certain metabolic pathways allows for personalized drug therapy, minimizing the risk of adverse interactions. The role of clinical pharmacy extends beyond conventional practices, incorporating genomics to optimize patient-specific treatment plans (Bojuwoye et al., 2022).

Bioavailability, the extent to which a drug reaches the systemic circulation, is a critical factor in determining therapeutic efficacy. Clinical pharmacists, well-versed in the nuances of absorption mechanisms, contribute significantly to recognizing and managing DDIs related to bioavailability (Leenhardt et al., 2021).

The absorption of drugs from the gastrointestinal tract is a complex process influenced by factors such as drug formulation, food interactions, and the presence of other medications. Clinical pharmacists meticulously assess these variables, recognizing potential challenges in bioavailability that may arise due to concurrent drug administration (Mahmoudjafari et al., 2020).

Clinical pharmacists are instrumental in educating patients about the impact of food on drug absorption. Certain medications exhibit altered bioavailability in the presence of specific dietary components. Through patient counseling and collaborative care, clinical pharmacists navigate food-drug interactions, ensuring optimal drug absorption and therapeutic outcomes (Nimee et al., 2022).

Once absorbed, drugs traverse the bloodstream, with their distribution influenced by physiological factors and interactions with other medications. Clinical pharmacy interventions in this realm encompass an understanding of distribution dynamics and their implications for DDIs (Ramos et al., 2018).

Many drugs bind to plasma proteins, influencing their distribution and availability at the target site. Clinical pharmacists, cognizant of the potential for drug displacement from protein binding sites, assess the cumulative effects of co-administered medications. This awareness allows for the identification of DDIs that may alter the free fraction of drugs in circulation, impacting their pharmacological activity (Ramos et al., 2018).

Research Questions

i. What are the most common potential drug-drug interactions among cardiology patients?

ii. What factors contribute to the increased risk of DDIs?

CHAPTER III

METHODOLOGY

This chapter provides details regarding the research design, participants or sample, data collection and analysis procedures, and the approach employed to analyze the findings.

Research Design

A retrospective observational study was conducted on patients (aged 18 and above) hospitalized at the cardiology department between December 1st, 2022, to December 1st, 2023 at the NEUH in the TRNC.

Inclusion Criteria

- Patients aged 18 years and above.
- Patients admitted to cardiology department
- Patients who are prescribed more than one medication

Exclusion Criteria

- Incomplete patient files

Sample Size and data collection

The Rao soft software calculator with 5% margin of error, 95% confidence level and 1000 population size were used to estimate the required sample size. The recommended sample size was 278. Data were collected from the medical records of all patients admitted to cardiology department for 12 months (Dec 1st, 2022, to Dec 1st, 2023). The nucleus program of the NEU hospital system was used to assist in collecting the data. The approximate time needed to complete the data collection for each patient was approximately 5 minutes. Patients' ages, genders, primary diagnoses, concurrent disease states and medications were recorded.

Statistical data analysis Procedure

Statistical methods were used to analyze the data, including the calculation of descriptive statistics such as the frequency and percentage for categorical variables, the weighted mean, the median, the standard deviation (SD), and the minimum and maximum for the continuous variables. To evaluate the associations between categorical variables, a Pearson Chi square test was performed. The level of significance was defined as $\alpha = 0.05$. All calculations and analyses were carried out with the SPSS (Statistical Package of Social Sciences Demo Version 22.0) program. Drugs.com and Medscape were used to analyze drug-drug interactions.

Ethical Considerations

Ethical approval for this research study was approved on 30th November 2023 from the Scientific Research Ethical Committee of Near East University Hospital (NEU/2022/108-1637). Throughout the study, strict measures were taken to ensure patient privacy and confidentiality. No private patient information was recorded. The study solely utilized patients' file numbers, age, gender, diagnosis, and medications as data points.

CHAPTER IV

RESULTS

Demographic characteristics for the patients

A total of 288 patients were included in the analysis to check the interaction between drugs according to drugs.com and Medscape. The majority of the patients were males (171, 59.4%) and (117, 40.6%) were females. The mean age for the patients was (72.8±13.8). The length of stay for patients was ranged from one day to 29 days with mean (5.7±3.7). Coronary artery disease was the most common disease that leads patients to enter ICU (78, 27.1%) followed by hypertension (38, 13.1%).

Table 1. Demographic characteristics for the patients.

	Characteristics	**N**	**%**
Gender	**Male**	171	59.4
	Female	117	40.6
Age group	**27-44**	13	4.5
	45-64	50	17.4
	65-	225	78.1
	Total	288	100
Admission diseases	**Coronary artery disease**	78	27.1
	Hypertension	38	13.1
Age (mean ± SD)	72.8±13.8		
Length of stay in days (mean ± SD)	5.7±3.7		

Drug interactions

Regarding the mechanism of interaction, the majority of the interactions (138, 47.9%) were identified as pharmacodynamic based on dugs.com. Pharmacokinetics interactions were identified in (94, 32.6%) out of the interactions. Regarding the mechanism of interaction in Medscape, the majority of the interactions (135, 46.9%) were identified as pharmacodynamic based on Medscape. Pharmacokinetics interactions were identified in (90, 31.3%) out of the

interactions. Further details about mechanism of interaction in both drugs.com and Medscape are provided in table 2.

Table 2. Mechanism of interactions in both Drugs.com and Medscape

		N	%
Drugs.com	No interaction	56	19.4
	PD	138	47.9
	PK	94	32.6
	Total	288	100.0
Medscape	No interaction	63	21.9
	PD	135	46.9
	PK	90	31.3
	Total	288	100.0

According to Drugs.com the interaction type was categorized into three categories as following: minor, moderate and major. In Medscape the pattern little differs, the interactions categorized into: minor, monitor closely, serious and contraindicated.

Our data showed that the number of minor interactions in drugs.com and Medscape was (2, 0.7%) and (49, 17%), respectively. The majority of interactions was moderate according to drugs.com (131, 45.5%), while in Medscape was serious (88, 30.6%) interaction. Further details about interaction categories in both drugs.com and Medscape are provided in table 3.

Table 3. Drugs interaction

	Interaction type	N	%
Drugs.com	**No interaction**	56	19.4%
	Minor	2	0.7%
	Moderate	131	45.5%
	Major	99	34.4%
Medscape	**No interaction**	59	20.5%
	Minor	49	17.0%
	Monitor closely	87	30.2%
	Serious	88	30.6%
	Contraindicated	5	1.7%

In the analysis the most common interaction was recorded according the number of interactions in the two different tools, drugs.com recorded 232 interactions were found (80.5%), while Medscape recorded 229 interactions among 288 patients (79.5%).

The most common major interactions according to Drugs.com were between NSAIDs +Anticoagulant (16 DDIs) which increase the risk of serious bleeding and managed by avoid this type of interactions as possible. Minor interactions were occurred twice by acetaminophen + scopolamine and CCB +ACEi and no need for any management. Further details about drug interaction in drugs.com are provided in table 4.

Table 4. The classification of interactions according to Drugs.com

	Severity	**Most common DDI**	**Effects**	**Managements**
Drugs.com	**Major Interaction**	NSAIDs +Anticoagulant (16 DDIs)**	Increase the risk of serious bleeding	Avoid combination
		Antiarrhythmic + Loop Diuretics (9 DDIs)	Prolongation of the QT interval	Avoid combination
	Moderate Interaction	Loop diuretic +BB (25 DDIs)	Together may lower your blood pressure	Monitor the patient BP.
		NSAIDs +Anticoagulan (13 DDIs)	Increase the risk of serious bleeding	Try to change the NSAIDs
	Minor Interaction	Acetaminophen +Scopolamine (1 DDIs)	Decrease the gastrointestinal absorption of acetaminophen	-
		CCB +ACEi (1 DDIs)	may have additive hypotensive effects	-

The most common moderate interactions according to Drugs.com were in beta blockers, Loop diuretics and antibiotics (13, 11.0%) (12, 10.2%) (10, 8.5%), respectively. In major interactions drug groups, the most common groups were Anticoagulant, antipsychotics and antibiotics (20, 18.9%) (10, 9.4%) (9, 8.5%), respectively. Further details about common drug interaction in drugs.com are provided in tables 5 and 6.

Table 5. The most common drugs group had moderate interactions according to Drugs.com

Drug group	N	%
Beta Blockers	13	11.0
Loop diuretic	12	10.2
Antibiotics	10	8.5
NSAIDs	9	7.6
Anticoagulant	8	6.8
ACE	7	5.9
Anti-Diabetic	7	5.9
Antipsychotic	7	5.9
CCBs	6	5.1
ARBs	4	3.4
Statin	4	3.4
Cortisone	3	2.5
doxazosin	3	2.5
PPI	3	2.5
Thiazides	2	1.7
Antiarrhythmic	2	1.7
digoxin	2	1.7
Other	16	13.6
Total	**118**	**100**

Table 6. The most common drugs group had major interactions according to Drugs.com

Drug group	N	%
Anticoagulant	20	18.9
Anti-Psychotic	10	9.4
Antibiotics	9	8.5
ACE	7	6.6
Antiarrhythmic	7	6.6
ARB	5	4.7
Antiplatelet	5	4.7
Potassium sparing	5	4.7
Statin	4	3.8
colchicine	3	2.8
Cortisone	3	2.8
Anti-Diabetic	2	1.9
allopurinol	2	1.9
Beta blockers	2	1.9
CCB	2	1.9
Loop diuretics	2	1.9
NSAIDs	2	1.9
Others	16	15.1
	106	100

According Drugs.com, regarding the age group and interaction, the interaction increased significantly in the elderly patients compared to younger. In details, 8 (3.4%) interaction were found in the age group 27-44 years old, while 186 (80.2%) interaction were occurred in the patients more than 65 years old (p =0.04).

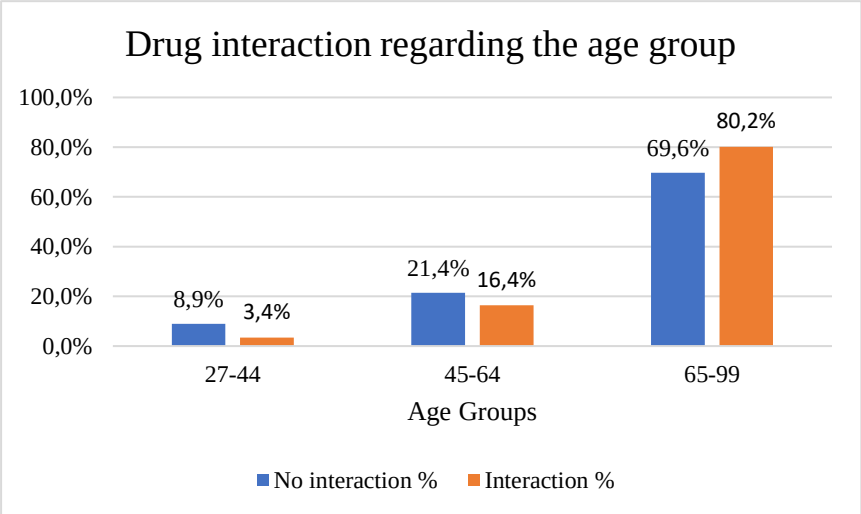

Figure 1. Drug interactions among age groups

The gender of the patients showed that only 62.1% of the interaction were found in males, 37.9% interaction were in females. The below table demonstrated that there is a significant association between interaction and gender (X^2 = 3.5 p=0.05).

Table 7. The interaction according Drugs.com and gender

		Drugs.com				Total	
		No interaction		Interaction			
		N	%	N	%	N	%
Gender	Male	27	48.2%	144	62.1%	171	59.4%
	Female	29	51.8%	88	37.9%	117	40.6%
Total		56	100.0%	232	100.0%	288	100.0%

According Medscape, regarding the age group and interaction, the interaction increased insignificantly in the elderly patients compared to younger. In details, 9 (3.9%) interaction were found in the age group 27-44 years old, while 184 (80.2%) interaction were occurred in the patients more than 65 years old (p =0.19).

The most common contraindicated interactions according to Medscape were between Anticoagulant + Antiplatelets (2 DDIs) which increase the risk of serious bleeding and

managed by avoid this type of interactions as possible. Minor interactions were occurred twice by Cephalosporin + Loop (9 DDIs) and Cortisone + Loop diuretics (5 DDIs) which can both may affect the kidney electrolyte balance and fluid status, respectively and no need for any management. Further details about drug interaction in Medscape are provided in table 8.

Table 8. The classification of interactions according to Medscape

	Severity	**Most common DDI**	**Effects**	**Managements**
Medscape	**Contraindicated**	Anticoagulants + Antiplatelets (2 DDIs)	Increase the risk of bleeding	Avoid combination
	Serious	Anticoagulant + ACEi (22 DDIs)	Together may lower your blood pressure	Monitor the patient BP.
		Cephalosporin +Anticoagulants (17 DDIs)	Increase the risk of serious bleeding	Try to change the Cephalosporin or monitor closely
	Monitor Closely	NSAIDs + Anticoagulant (8 DDIs)	Increase the risk of serious bleeding	Monitor the patients for any signs of bleeding
		NSAIDs +Antiplatelet (6 DDIs)	Increase the risk of serious bleeding	Monitor the patients for any signs of bleeding or change the NSIADs.
	Minor	Cephalosporin + Loop (9 DDIs)	Both may affect the kidney	-
		Cortisone + Loop (5 DDIs)	electrolyte balance and fluid status	-

The most common contraindicated interactions according to Medscape were in Anticoagulant, (3, 30%). In serious interactions drug groups, the most common groups were Anticoagulant, antipsychotics and antibiotics (14, 20.6%) (7, 10.3%) (6, 8.8%), respectively. Monitor closely interactions were occurred almost in Anticoagulant, loop diuretics and NSAIDs (11, 11.5%)

(10, 10.4%) and (10, 10.4%), respectively. Further details about drug interactions group in Medscape are provided in tables 9,10,11 and 12.

Table 9. The most common drugs group had contraindicated interactions according to Medscape

	N	%
Anticoagulant	3	30
Other	7	70
Total	**10**	**100**

Table 10. The most common drugs group had serious interactions according to Medscape

	N	%
Anticoagulant	14	20.6
Anti-Psychotic	7	10.3
Anti-biotics	6	8.8
Beta blockers	4	5.9
ACEi	3	4.4
Antiplatelet	3	4.4
General Anesthetic	3	4.4
Statins	3	4.4
ARBs	2	2.9
Antiarrhythmic	2	2.9
CCB	2	2.9
Steroids	2	2.9
Digoxin	2	2.9
PPIs	2	2.9
Other	13	19.1
Total	**68**	**100**

Table 11. The most common drugs group had monitor closely interactions according to Medscape

	N	**%**
Anticoagulant	11	11.5
Loop diuretics	10	10.4
NSAIDs	10	10.4
Beta blockers	9	9.4
CCB	7	7.3
Antiarrhythmic	6	6.3
Antipsychotic	6	6.3
Antibiotics	5	5.2

Statin	5	5.2
Antiplatelet	4	4.2
ARBs	4	4.2
ACEi	3	3.1
Anti-Diabetics	3	3.1
Alpha blockers	2	2.1
PPI	2	2.1
Potassium sparing	2	2.1
Others	7	7.3
Total	**96**	**100**

Table 12. The most common drugs group had minor interactions according to Medscape

	N	**%**
Anti-biotics	4	8.7
Anti-Diabetics	3	6.5
Antiplatelet	1	2.2
Anti-psychotics	2	4.3
Thyroids	2	4.3
Beta Blockers	2	4.3
CCB	3	6.5
Cortisone	4	8.7
B12	2	4.3
Loop diuretics	9	19.6
NSAIDs	4	8.7
PPI	3	6.5
Thiazides	2	4.3
Others	5	10.9
Total	**46**	**100**

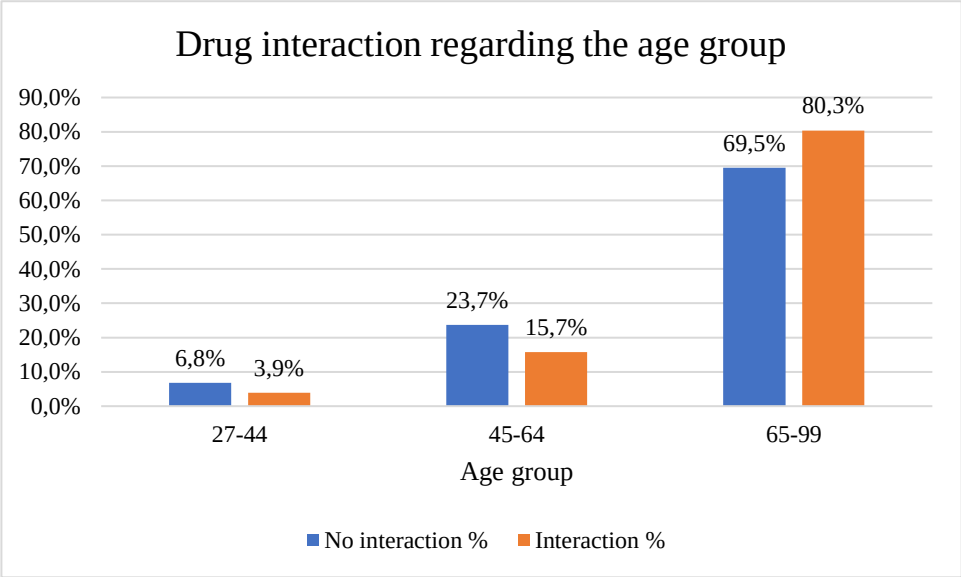

Figure 2. Drug interactions among age groups in Medscape

The gender of the patients showed that only 60.7% of the interaction were found in males, 39.3% interaction were in females. The below table demonstrated that there is insignificant association between interaction and gender (X2 = .8 p=0.36).

Table 13. The interaction according Medscape and gender

		Medscape				Total	
		No interaction		Interaction			
		N	%	N	%	N	%
Gender	Male	32	54.2%	139	60.7%	171	59.4%
	Female	27	45.8%	90	39.3%	117	40.6%
Total		59	100.0%	229	100.0%	288	100.0%

CHAPTER V

DISCUSSION

Drug-drug interactions (DDI) have recently received much attention from the regulatory, scientific and health communities worldwide. In medical practice, it is quite common to use drug combinations with the potential for interaction, and although not all DDIs observed in a patient may occur (potential DDIs), their identification is essential because they may increase the risk of side effects.). , toxicity or reduction in therapeutic efficacy, which, in addition to adverse outcomes for patients, can increase hospital length of stay and costs.

Our study showed that in the cardiology clinic around 80% interaction was recorded, these findings showed that there is a potential interaction. This high percentage increase the demands to establish an application to avoid any interaction that leads to increase the length of stay for the patients or increase the cost or even affect the treatment efficacy.

Our high incidence of interaction was not in the same line with other studies, for instance a study showed the mean number of DDIs per 1000 medication administrations was 70.1, dropping to 31.0 when considering only clinically relevant potential DDIs. In total, 53.8% of the ICU patients was exposed to a potential DDI and 38.2% to a clinically relevant potential DDI. The difference between our findings and these may relate to the health system and the pharmacist play a critical role in their clinics. (Bakker, T., et al, 2021)

This single-center study by Askari et al. identified on average 1.7 DDIs per ICU admission, slightly higher compared to our findings. Differences in clinical relevance definition and detection methods may explain this. (Askari, M., et al., 2013)

The most common interaction found in our study was related to aspirin and amiodarone, these finding showed similarity with a large study conducted by Bakker, T., et al,. This similarity due to the prevalence of prescribing these drugs in CCU and the low high drug interactions associated with these medicines.

Our length of stay mean was 5.7 and the number of interactions among the patients was 229 interactions, which is more than 80% of the patients has at least one interaction. Previous published articles showed that a relatively low prevalence rate of DDI among CCU patients 40% − 79.5%, and in another study, 84.2% of CCU patients developed at least one relevant DDI (Smithburger, P. L., et al., 2010) (Farzanegan, B., el., 2015) & (Wang, H., et al., 2022). The difference between our study, Chinese study and he others mainly related to the sample size and the enrolled patients in the analysis.

This study has some limitations. Since the study design was retrospective, we could not ascertain with any accurate completeness or reliability of the information obtained. As such, it was possible that we could have under- or over-reported the DDIs.

As some drugs were prescribed to be taken as required, we could not accurately determine whether these drugs were actually taken with others, which is difficult to make the assessment of drug–drug interaction.

One of the major limitations of this study is different factors that affect the prevalence of interaction was not taken in consideration such as patients weight, genetic factors, major organ function status, and drug compliance.

Another limitation is that this study took place in single hospital so the findings may be unable to be generalized. Also, this study evaluated one interaction among CCU patients, study will be stronger if more than one interaction included and how affect the length of stay.

CHAPTER VI

CONCLUSION

The most common drug interaction in hospitalized patients were occurred in CCU, generally due to high alert medication prescribed for these patients. Our findings showed that the number of drug interaction was detected higher using drugs.com compared to Medscape. To keep the efficacy of the treatment and reduced adverse drug reactions, physicians and drug prescriber must be trained about using applications to avoid any interaction not only by altering the drug but by monitoring or decreasing the dose or increasing the interval as these applications suggested.

Regular training on the appropriate use of these applications by physicians and healthcare providers is crucial to maintaining treatment efficacy and reducing the risk of adverse medication responses. They should think about alternative tactics recommended by these tools, like modifying dosages, closely monitoring patients, or prolonging dosing intervals, rather than merely making simple changes to medication regimens. While ensuring that therapeutic goals are met, these approaches can assist reduce the hazards associated with interactions.

The study does, however, also highlight the necessity of more investigation in this field. To assess the comprehensiveness and accuracy of a wider variety of drug interaction checking techniques, further research needs to be done. Furthermore, to be sure that more recent methods can consistently identify interactions that are clinically meaningful, it is crucial to validate them. Subsequent investigations ought to delve into the practical consequences of employing diverse interaction checkers and investigate if incorporating these instruments into clinical procedures in a more methodical manner will enhance patient results and safety.

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