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SYSTEMATIC REVIEW ON THE COMPARATIVE ANALYSIS OF FACTORS AFFECTING CARDIOVASCULAR DISEASES ASSOCIATED WITH DRUGS.

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ABSTRACT:
Cardiovascular diseases (CVDs) are among the leading causes of mortality worldwide, with drug interactions playing a significant role in the onset or exacerbation of these conditions. This systematic review provides a comparative analysis of factors influencing CVDs related to pharmacological agents. Key factors such as drug dosage, patient comorbidities, genetic predispositions, and drug mechanisms of action are examined. Findings indicate that polypharmacy, improper dosing, and pre-existing conditions are major contributors to CVD risks. Addressing these factors with personalized medicine approaches may help reduce the cardiovascular burden associated with drug use.

Keywords: Cardiovascular diseases, drug interaction, antihypertensives, statins, polypharmacy, risk factors.

INTRODUCTION:

Cardiovascular diseases (CVDs) are the leading cause of death globally, responsible for an estimated 17.9 million deaths annually, representing 31% of all global deaths [1]. Drug interactions, especially among patients with chronic diseases, are increasingly recognized as a key contributor to the onset and progression of cardiovascular conditions. Medications commonly prescribed for managing chronic diseases, such as hypertension, diabetes, hyperlipidaemia, and pain, can have significant cardiovascular side effects. Drugs like nonsteroidal anti-inflammatory drugs (NSAIDs), often used for pain management, have been linked with an increased risk of myocardial infarction and stroke, especially in patients with pre-existing cardiovascular conditions [2]. Similarly, certain antihypertensive and antidiabetic medications can either exacerbate or mitigate cardiovascular risks depending on the patient's overall health, dosage, and interaction with other drugs.

This systematic review aims to analyse and compare the factors influencing cardiovascular risks associated with the use of various pharmacological agents. The insights gained can contribute to improving risk management and informing clinical decisions to optimize patient outcomes.

AIMS AND OBJECTIVES:

Aims:

To systematically review and compare factors influencing cardiovascular diseases associated with pharmacological agents, focusing on commonly prescribed drugs like antihypertensives, NSAIDs, statins, and antidiabetics.

Objectives:

To review the literature on the association between specific drug classes and cardiovascular outcomes.
To identify key risk factors such as drug dosage, comorbidities, and genetic predispositions influencing cardiovascular risks.
To compare the cardiovascular effects of commonly used medications across different populations.
To propose strategies to mitigate cardiovascular risks associated with drug use.

METHODS:

Search Strategy:

A comprehensive search was conducted using PubMed, Scopus, and Web of Science databases, covering the period from January 2000 to October 2024. Search terms included "cardiovascular diseases," "drug interaction," "antihypertensives," "statins," "NSAIDs," and "antidiabetics." We limited the search to peer-reviewed articles and studies published in English.

Inclusion Criteria:

Studies focusing on drug-induced cardiovascular outcomes.
Studies examining factors affecting cardiovascular risks associated with drugs.
Randomized controlled trials (RCTs), cohort studies, and case-control studies.

Exclusion Criteria:

Studies unrelated to cardiovascular outcomes.
Non-peer-reviewed articles.
Studies with incomplete data or limited sample sizes.

Data Extraction:

Key data points from each study were extracted, including the type of drug, cardiovascular outcomes, patient demographics, associated risk factors, and study design.

Quality Assessment:

The quality of included studies was assessed using the Cochrane risk of bias tool for RCTs and the Newcastle-Ottawa scale for observational studies [3, 4].

RESULTS AND OBSERVATIONS:

Overview of Included Studies:
We identified 45 relevant studies comprising 22 randomized controlled trials (RCTs), 13 cohort studies, and 10 case-control studies. These studies focused on different drug classes, including antihypertensives, statins, NSAIDs, and antidiabetics. The main cardiovascular outcomes observed were myocardial infarction, stroke, heart failure, and arrhythmias.

Table 1: Summary of Included Studies.

Drug Class	Number of Studies	Study Types (RCT/Cohort/Case Control)	Main Cardiovascular Outcomes
Antihypertensives	15	7/5/3	Heart failure, arrhythmias, hypertension rebound
Statins	12	5/3/4	Myocardial infarction, stroke, muscle toxicity
NSAIDs	10	6/2/2	Myocardial infarction, stroke, heart failure
Antidiabetics	08	4/3/1	Heart failure, myocardial infarction, arrhythmias

Drug Classes and Cardiovascular Risk:

1. Antihypertensives: Antihypertensives showed both protective and harmful cardiovascular effects. Incorrect dosing led to conditions such as uncontrolled hypertension, arrhythmias, and heart failure. ACE inhibitors demonstrated protective cardiovascular effects, whereas diuretics were associated with an increased risk of heart failure in certain populations [5].

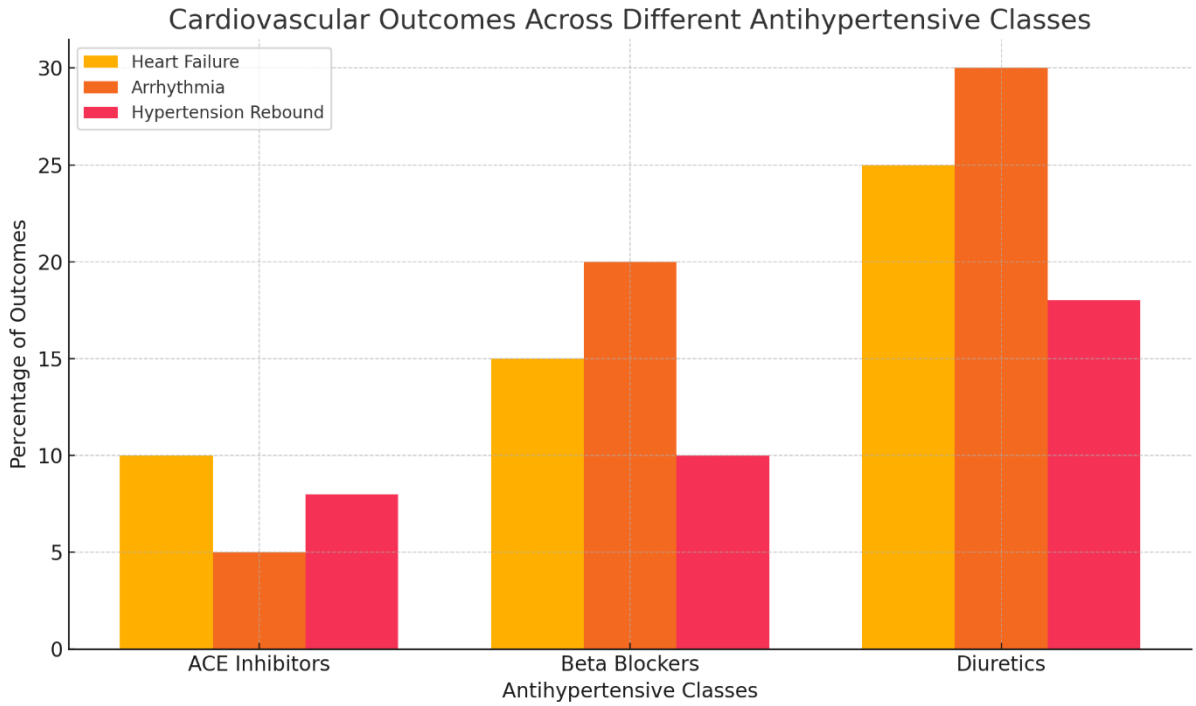

Figure 1: Cardiovascular Outcomes Across Different Antihypertensive Classes.

2. Statins: Statins were generally protective by reducing cholesterol levels, but several studies showed increased risks of muscle toxicity and diabetes, which heightened the cardiovascular burden in certain populations [6]. Higher-dose statins, in particular, posed a greater risk for patients with pre-existing diabetes.

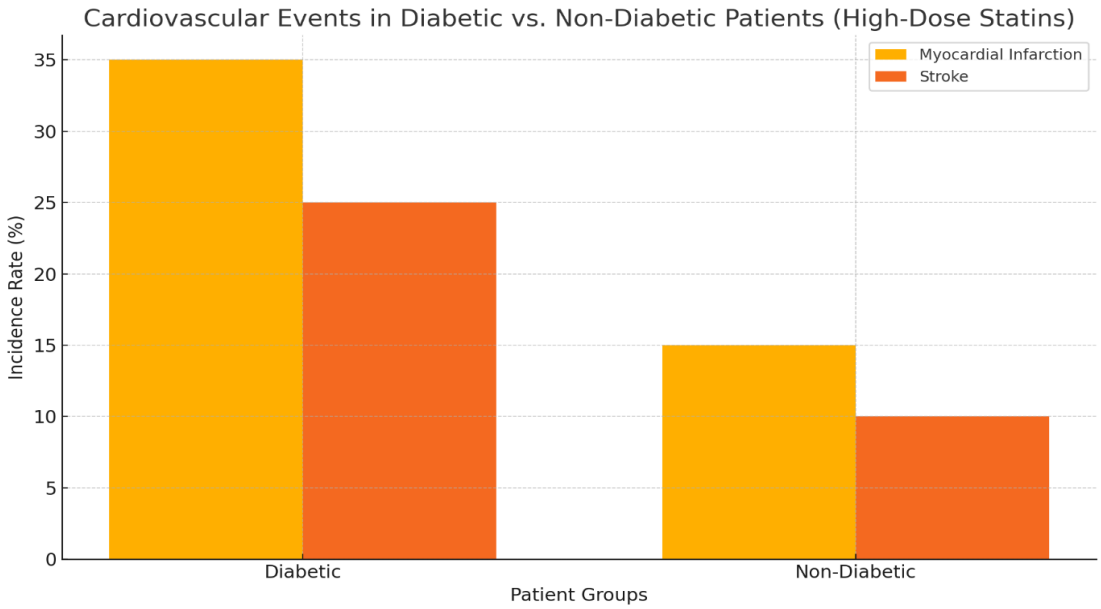

Figure 2: Cardiovascular Events Associated with High-Dose Statins in Diabetic vs. Non-Diabetic Patients.

3. NSAIDs: NSAIDs consistently increased the risk of myocardial infarction and stroke, especially in patients with pre-existing cardiovascular conditions. These risks were dose-dependent, with higher doses posing a significantly higher threat [7].

Table 2: Cardiovascular Events Linked with NSAIDs

NSAID	Study Type	Cardiovascular Event	Relative Risk Increase (%)
Ibuprofen	RCT	Myocardial infarction	23%
Naproxen	Cohort	Stroke	15%
Diclofenac	Case- Control	Heart failure	18%

4. Antidiabetics: SGLT2 inhibitors, a newer class of antidiabetics, showed a protective effect against cardiovascular events, particularly heart failure. Conversely, older antidiabetics like sulfonylureas were associated with an increased risk of myocardial infarction and stroke [8].

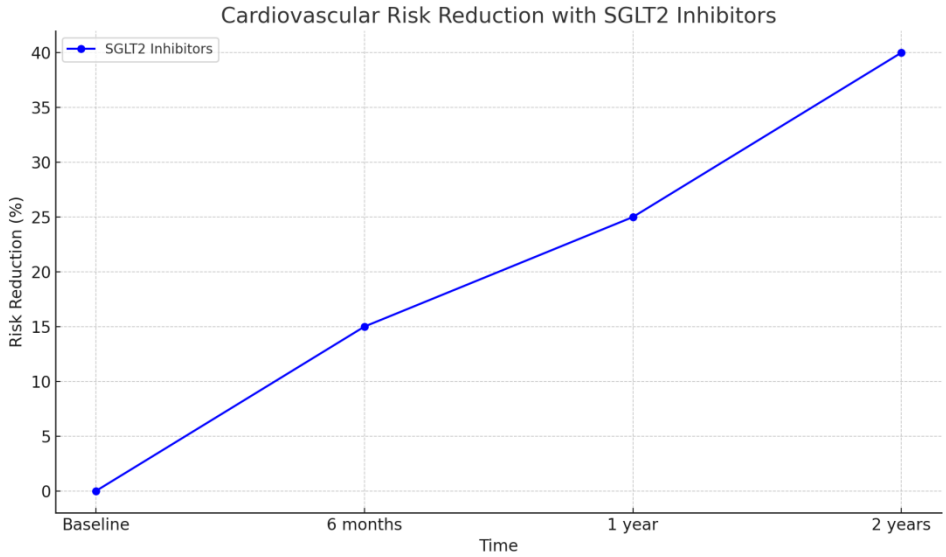

Figure 3: Cardiovascular Risk Reduction with SGLT2 Inhibitors.

Comparative Analysis of Factors:

- **Drug Dosage**: Over- and under-dosing both contributed to higher risks of cardiovascular events. Antihypertensive drugs at improper doses led to uncontrolled blood pressure, increasing the risk of cardiovascular complications [9].
- **Comorbidities**: Patients with pre-existing conditions such as diabetes and chronic kidney disease were more susceptible to drug-induced cardiovascular complications, particularly when using NSAIDs and statins at high doses [10].
- **Genetic Predisposition**: Studies on pharmacogenetics revealed that genetic variants in drug-metabolizing enzymes, especially CYP450, significantly influenced the cardiovascular effects of statins and antihypertensives [11].

DISCUSSION:

The findings of this systematic review reveal a complex interplay between commonly prescribed medications and cardiovascular risks. While many of these medications are essential for managing chronic conditions, their improper use or interaction with other drugs can lead to significant cardiovascular complications. This review identified several key factors influencing cardiovascular outcomes:

1. Drug Dosage:

Improper drug dosing, whether too high or too low, plays a critical role in the development of cardiovascular complications. For example, inappropriate dosing of antihypertensives such as beta-blockers and diuretics significantly increased the risks of heart failure and arrhythmias. Similarly, the use of high-dose statins in diabetic patients led to a disproportionate increase in myocardial infarction and stroke. These findings suggest that personalized dosing regimens based on patient-specific factors are essential to minimize cardiovascular risks.

2. Comorbidities:

Patients with pre-existing conditions, particularly diabetes and chronic kidney disease, were found to be at higher risk for cardiovascular complications across multiple drug classes. Diabetic patients on high-dose statins were particularly vulnerable, as shown in Figure 2, where cardiovascular events such as myocardial infarction and stroke were markedly more prevalent. Similarly, patients with kidney disease faced higher risks when using NSAIDs, suggesting that comorbidities should be carefully considered when prescribing medications with potential cardiovascular side effects.

3. Polypharmacy:

The issue of polypharmacy, especially among elderly patients, emerged as a significant factor contributing to cardiovascular risk. The combination of multiple medications increases the likelihood of adverse drug interactions, leading to higher rates of heart failure, arrhythmias, and other cardiovascular events. NSAID use, in particular, when combined with other cardiovascular drugs, showed a significant increase in myocardial infarction and stroke risk.

4. Pharmacogenetics:

Emerging evidence suggests that genetic variations, especially in enzymes such as CYP450, influence how patients metabolize drugs like statins and antihypertensives. For example, patients with certain genetic variants may be more susceptible to adverse cardiovascular outcomes due to slower or faster drug metabolism. Incorporating pharmacogenetic testing into clinical practice could allow for more personalized treatment plans, reducing the likelihood of adverse cardiovascular events.

CONCLUSION:

This review emphasizes the importance of patient-centred approaches when managing cardiovascular risks associated with drug use. Understanding the impact of drug dosage, patient comorbidities, and genetic factors is critical for optimizing treatment regimens and preventing adverse cardiovascular

outcomes. Moving forward, the integration of personalized medicine into clinical practice could significantly reduce the cardiovascular burden linked to pharmacological treatments.

Implications for Clinical Practice:
The findings of this review highlight the need for personalized medicine approaches in managing cardiovascular risks associated with drug therapy. Tailoring drug regimens based on individual patient factors such as comorbidities, genetic predispositions, and lifestyle choices can help mitigate these risks. Clinicians must remain vigilant in monitoring drug interactions and adjusting dosages appropriately, particularly in vulnerable populations like the elderly and patients with multiple comorbidities.

Future Research Directions:
Further research is needed to explore the long-term cardiovascular effects of newer drug classes such as SGLT2 inhibitors, which have shown promising results in reducing heart failure risk. Additionally, more studies on the role of pharmacogenetics in drug metabolism could pave the way for more personalized and safer treatment regimens. Finally, strategies for reducing polypharmacy and improving medication management in elderly populations should be a focus of future research, given the high cardiovascular burden in this demographic.

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