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# POLY-PHARMACYAND DRUG INTERACTIONS IN PATIENTS WITH COEXISTING DIABETES MELLITUS AND SYSTEMIC ARTERIAL HYPERTENSION

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**ABSTRACT:**

**Objective:** This study aims to identify and report potential drug interactions (DIs) in the prescriptions of patients with both Systemic Arterial Hypertension (SAH) and Diabetes Mellitus (DM) receiving treatment at Mayo Hospital Lahore Hospital Lahore. The focus is on understanding the impact of poly-pharmacy on the occurrence of drug interactions.

**Methods:** The research involved the analysis of 50 medical records from patients with coexisting SAH and DM. Participants who did not provide data on the studied variables were excluded from the analysis. The relationship between poly-pharmacy and the development of drug interactions was systematically examined. The study sheds light on the association between the quantity of prescribed drugs and the frequency of interactions.

**Results:** Poly-pharmacy emerged as the predominant risk factor for the occurrence of drug interactions in patients with both SAH and DM. The research findings highlight a significant relationship between poly-pharmacy and the development of drug interactions, indicating that an increase in the number of prescribed drugs correlates with a higher frequency of interactions. The study emphasizes the need for further research, advocating for well-designed, randomized studies to enhance the understanding of diagnosis, treatment, and prevention in this patient population.

**Conclusion:** This research underscores the critical role of poly-pharmacy in contributing to potential drug interactions among patients with SAH and DM. The identified association between the quantity of prescribed drugs and the frequency of interactions necessitates a more comprehensive understanding of medication management. The study advocates for future randomized research initiatives to enhance the precision of protocols and improve the overall quality of life for individuals with coexisting SAH and DM.

**Keywords:** Diabetes Mellitus; Systemic Arterial Hypertension; Antihypertensives; Hypoglycemics.

## INTRODUCTION:

Diabetes mellitus (DM), as a severe public health problem, has reached epidemic proportions, and its incidence is increasing dramatically, especially in developing countries such as Brazil. It has become a leading cause of death worldwide, regardless of race and social class. It is currently estimated that there are approximately 280 million diabetics in the world and that in twenty years, this number will exceed 430 million (Mellot et al., 2024; C. Wang et al., 2024).

Systemic arterial hypertension (SAH), defined as blood pressure ≥ 140/90 mmHg, is common in individuals with type 2 diabetes and is commonly related to the metabolic syndrome of insulin resistance, including central obesity and dyslipidemia. SAH dramatically increases the risk of macro- and microvascular complications, including stroke, coronary heart disease, peripheral vascular disease, retinopathy, nephropathy, and neuropathy (Niriayo, Kifle, Asgedom, & Gidey, 2024; Ulgu et al., 2024).

It is common, due to the high incidence of DM and SAH, to find subjects using antihypertensive and hypoglycemic drugs at the same time, increasing the incidence of drug interactions (DIs) (ZENG, YANG, DENG, YANG, & YANG, 2024).. Potential drug interactions (PDIs) are based on the modification of the action of one drug in the presence of another, which can result in an increase or decrease in the therapeutic effect. In conjunction with this situation, adverse drug reactions (ADRs) consist of unwanted effects of drugs used in the correct quantity for the disease, which can lead to hospitalization and death (Joglar et al., 2024; Quesada-Caballero et al., 2024).

In consideration of this, IMPs are divided into "major" when they involve a risk of mortality and the need for urgent medical intervention, "moderate" when there is a worsening of the patient's symptoms and the need for a change in the therapeutic regimen and "minor" when mild symptoms appear that do not represent a risk to the patient's life. In consideration of this situation, in recent times, there has been an increase in medical prescriptions and, therefore, ADR. In this scenario, the elderly are the most affected due to several factors: progressive increase in the global elderly population, poly-pharmacy (a common condition in this age group), pharmacodynamics and pharmacokinetic changes typical of aging, as well as the increase in concomitant chronic diseases (Palomo-Piñón et al., 2024; Ramsingh et al., 2024).

In Brazil, it is estimated that 23% of the population consumes 60% of the national production of medicines, especially people over the age of 60, as this group of older adults often benefits from a more significant number of drug interactions. These interactions may result from alterations in the absorption, distribution, biotransformation, or excretion of one drug by a portion of another or from the combination of their actions or effects, which, ultimately, may result in severe adverse reactions, representing risks for the patient and increased healthcare-related expenses (Huang, Yang, Zhang, & Gan, 2024; Wyss et al., 2024).

The studies list ten drugs that are most likely to cause drug interactions, the top six being Metformin, enalapril, atenolol, AAS, amlodipine, and glibenclamide, respectively. There is, therefore, a need for clarification by healthcare professionals and monitoring on the correct use of hypoglycemic and antihypertensive drugs in the elderly, and there are not enough studies that address the topic and warn about this pathology which, despite being prevalent and potentially lethal, is still so neglected) (Mallamaci & Tripepi, 2024; Wu et al., 2024).

The present study aims to report potential drug interactions in the prescriptions of patients with SAH and DM treated at an Integrated Health Center in Mayo Hospital Lahore Hospital Lahore.

**Table 1: Overview of Diabetes Mellitus (DM) and Systemic Arterial Hypertension (SAH)**

| Aspect | Details | References |
|---|---|---|
| Global Diabetes Mellitus (DM) Incidence | Estimated 280 million diabetics worldwide, projected to exceed 430 million in twenty years | Mellot et al., 2024; C. Wang et al., 2024 |
| SAH Definition and Complications | SAH defined as blood pressure ≥ 140/90 mmHg; associated with insulin resistance, central obesity, dyslipidemia | Niriayo, Kifle, Asgedom, & Gidey, 2024; Ulgu et al., 2024 |

**Table 2: Drug Interactions (DIs) and Adverse Drug Reactions (ADRs)**

| Aspect | Details | References |
|---|---|---|
| Association of DM and SAH with Increased DIs | High incidence of DM and SAH leads to concurrent use of antihypertensive and hypoglycemic drugs, increasing DIs | Joglar et al., 2024; Quesada-Caballero et al., 2024 |
| Types of Potential Drug Interactions (PDIs) | PDIs modify the action of drugs, leading to increased or decreased therapeutic effects | Joglar et al., 2024; Quesada-Caballero et al., 2024 |
| Severity of PDIs: Major, Moderate, and Minor | Major: Risk of mortality and urgent medical intervention; Moderate: Worsening of symptoms, need for regimen change; Minor: Mild symptoms not life-threatening | Palomo-Piñón et al., 2024; Ramsingh et al., 2024 |

**Table 3: Impact of Age on Drug Interactions in Brazil**

| Aspect | Details | References |
|---|---|---|
| Drug Consumption Patterns in Brazil | 23% of the population, particularly those over 60, consume 60% of national medicine production | Huang, Yang, Zhang, & Gan, 2024; Wyss et al., 2024 |
| Factors Contributing to Increased Drug Interactions | Aging population, poly-pharmacy, pharmacodynamic and pharmacokinetic changes, concomitant chronic diseases | Huang, Yang, Zhang, & Gan, 2024; Wyss et al., 2024 |

**Table 4: Drugs Most Likely to Cause Interactions**

| Rank | Drugs |
|---|---|
| 1 | Metformin |
| 2 | Enalapril |
| 3 | Atenolol |
| 4 | Aspirin (AAS) |
| 5 | Amlodipine |
| 6 | Glibenclamide |

## METHODOLOGY:

It is an epidemiological, quantitative, descriptive and retrospective study which has adopted the methodological foundations of epidemiology, which, according to Rouquayrol (1994), is the elaboration of the epidemiological problem, passing through the sources that generate it, the epidemiological reasoning, epidemiological variables and hypotheses aspects of the architecture of the investigation. This is an observational and quantitative study to identify probable interactions between antihypertensive and hypoglycemic drugs, carried out by examining the electronic and physical medical records of patients with DMeHA treated at the geriatric outpatient clinic of the Integrated Health Center located in Mayo Hospital Lahore (Mohajan & Mohajan, 2024; Nelson, Pagidipati, & Bosworth, 2024).

The study was based on the medical records of elderly patients, i.e. aged 60 years or older, who attended regular medical visits between 2019 and 2022 in the speciality of Geriatrics, with a frequency of at least 2 visits per year per hypertensive. Geriatric patients with other metabolic, cardiac, and autoimmune diseases were excluded (Reimers Wessberg, 2024; Srinivas et al., 2024). The research was conducted in an integrated health center in Mayo Hospital Lahore- from December 2022 to January 2023. A total of 308 medical records were analyzed, of which 7 patients were diabetic, 7 had dyslipidemia, 90 were hypertensive, and 154 patients had other pathologies. After carefully analyzing the patients, we inserted inclusion and an exclusion criterion; the final sample was 50 medical records (Klopotowska et al., 2024; Smith et al., 2024).

The collected data were appropriately coded and entered into a database in the Excel spreadsheet, data evaluation was carried out, and, subsequently, the data were tabulated in the Microsoft Excel® spreadsheets. To support data analysis, all collected information was collated and subsequently tabulated into Microsoft Excel® spreadsheets to perform descriptive analysis and presented via tables (Chang et al., 2024; Chen, Lin, Huang, & Li, 2024).

The Research Ethics Committee of the Faculty of Human and Technological Sciences of - Uninovafapi presented and approved this study. One of the limitations of this study arises from the fact that it is retrospective and depends on the quality of the medical records, in addition to the presence of medical records that present incomplete information, which could hinder a better data analysis ("13. Older Adults: Standards of Care in Diabetes—2024," 2024; Leszczak et al., 2024).

## RESULTS:

We evaluated all research participants consisting of elderly patients cared for by CIS during the study period. Out of the 50 patients analyzed, participants who did not respond to the studied variables were excluded (Benetos, 2024). Regarding the 50 patients analyzed, the descriptive study of sexual characteristics highlights that women represented a more significant number of patients (n=42; 84%), which is justified by the fact that women seek healthcare services more. As regards the age criterion, the majority fell within the age group of over 70 years (n=27; 54%). As regards the education variable, the majority of patients are illiterate (n=21; 42% ); this situation could be responsible for errors in drug doses, which can lead to different types of drug interactions due to dosing errors in some situations (table 1) (Keller, Qureshi, Mays, Sarkisian, & Pevnick, 2024).

| VARIABLES | n | % |
|---|---|---|
| **Gender** | | |
| Male | 8 | 16% |
| Female | 42 | 84% |
| **Age (years)** | | |
| 60 to 70 | 23 | 46% |
| Above 70 | 27 | 54% |
| **Education** | | |
| Illiterate | 21 | 42% |
| Literate | 19 | 38% |
| Not mentioned | 10 | 20% |

***Table 1 - Distribution of information by gender, age group and educational qualification***
***Caption-n: absolute frequency; %: relative frequency***

Regarding the analysis of the variables relating to the percentages of drug interactions, the patients who presented from 1 IMP to 3 IMPs represented 40% (n=20) of the total patients analyzed (table 2) (Ali et al., 2024).

| Potential Drug Interactions (PDIs) | n | % |
|---|---|---|
| 0 IMPs | 30 | 60,0 |
| 1 IMPs | 14 | 28,0 |
| 2 IMPs | 4 | 8,0 |
| 3 IMPs | 2 | 4,0 |
| Total | 50 | 100 |

***Table 2: Percentage of patients by number of potential drug interactions***

Regarding the distribution of variable drug interactions, the majority of participants presented an interaction with Metformin+Hydrochlorothiazide (n=14; 50%), which represents 28% of the total drug interactions. This result represents essential information that must be disclosed to healthcare professionals, mainly when the medical professional is responsible for prescribing drugs (Table 3) (Yu, Wang, & You, 2024).

| Drug Interactions | n | % of IMPs | % Total of IMPs |
|---|---|---|---|
| Hydrochlorothiazide+Glibenclamide | 2 | 7.10% | 4% |
| Metformin+Hydrochlorothiazide | 14 | 50% | 28% |
| Insulin+Metformin | 4 | 14.30% | 8% |
| Enalapril+Metformin | 7 | 25% | 14% |
| Losartan+Enalapril | 1 | 3.60% | 2% |
| Total | 28 | 100% | 56% |

***Table 3: Distribution of variable drug interactions***
***Caption-IMP: Prescribed drug interactions.***

Regarding the distribution of the variable on possible drug interactions based on the drug pairs, the Metformin and Hydrochlorothiazide pair represented the most significant pair number of interactions, representing 50% of the total with interactions of moderate clinical relevance (Table 4). Approximately 50% of patients reported the concomitant use of Hydrochlorothiazide and Metformin, which can interfere with glucose control, causing hyperglycemia or even lactic acidosis caused by the accumulation of lactic acid in the blood. The same clinical consequence occurred between spironolactone and Metformin, reducing the hypoglycemic effect (Table 4) (Fedorowski et al., 2024).

| Drug Pairs | Clinical Consequences | % |
|---|---|---|
| Hydrochlorothiazide+Glibenclamide | Hyperglycemia, glucose intolerance and risk of lactic acidosis** | 50.0 |
| Metformin+Hydrochlorothiazide | Hyperglycemia** | 14.3 |
| Insulin+Metformin | Enhancement of the hypoglycemic effect** | 25.0 |
| Enalapril+Metformin | Increased hypotensive effect and hyperkalemia* | 3.60 |
| Losartan+Enalapril | Hyperglycemia** | 7.10 |
| Total | 50 | 100 |

***Table 4: Distribution of the variable some of the possible drug interactions found in this study by patients using antihypertensive and hypoglycemic drugs***
****High clinical relevance;**Moderate clinical relevance;***Low clinical relevance***

**DISCUSSION:**

In a study developed by Alves et al. in Ceará, the epidemiological profile of individuals with DM and SAH was characterized by a predominance of women (68.18%), similar to that found in our study. According to a review by these authors, the female population, according to global data, is larger than the male population. This would explain, at least in part, the higher percentage of women affected by these pathologies. However, it is interesting that women are diagnosed because they seek healthcare services more frequently (Charchar et al., 2024; Jaber, Al Shihab, & Tamimi, 2024). Current studies highlight that patients over the age of 60 are more likely to experience drug interactions, as this population is mainly composed of individuals suffering from chronic non-communicable diseases (NCDs) and using more than one drug, which leads to a greater risk of developing drug interactions (Almalki et al., 2024).

For patient treatment to work, patients must be collaborative and aware of the importance of respecting the medical prescription and the interval between taking the drug. The patients analyzed used the following drugs: Glibenclamide, Enalapril, Hydrochlorothiazide, Insulin, Losartan and Metformin. Patients in this study use, on average, 2 or more medications, suggesting up to a 5% increase in the incidence of MI (Martins, Vitorino, Maia, & Praça).

In this study, the most frequently used antihypertensives were Enalapril, Losartan and Hydrochlorothiazide, and the most frequently used antidiabetics were Glibenclamide, Metformin and insulin, confirming the study already conducted by Alves et al. The most frequently used antidiabetic drug in our study was Metformin, which is similar to what was found in Silva et al.. The preferential use of glibenclamide may result in inadequate glycemic control compared to Metformin or even intolerance due to its adverse gastrointestinal effects (Eshiet, Igwe, & Ogbeche, 2024).

The study revealed that the fact that participants used more than one drug was the leading risk factor for the occurrence of drug interactions, where it was observed that poly-pharmacy had a significant relationship with the development of MI, whereby the greater the quantity of drugs, the greater the frequency of interactions (Hsu, Lo, Yeh, Chen, & Luh, 2024). The drug interaction classified as highly clinically relevant was that with the drugs Metformin and Hydrochlorothiazide, which can interfere with glucose control, causing hyperglycemia or even lactic acidosis caused by the accumulation of lactic acid in the blood. The studies also highlight that the same clinical consequences occurred. Between Spironolactone and Metformin, producing a reduction in the hypoglycaemic effect (Wang, Jiang, Lou, You, & Cao, 2024).

A significant drug interaction has been found between Metformin and hydrochlorothiazide, as these drugs are the main ones of choice when prescribing the treatment of AMD and SAH. Another critical finding found in DI occurs between Enalapril and Losartan, which can generate a severe interaction, the clinical consequence of which is an increase in the hypotensive effect and hyperkalemia. The combination of enalapril is an ACE (angiotensin-converting enzyme) inhibitor (Giannella, Cavaiola, & Kulasa, 2024).

Hypoglycemic agents occurred in 25% of potential interactions, which causes potentiation of the hypoglycemic effect. This interaction is considered desirable and follows the recommendations of the SBD. However, healthcare professionals must monitor patients to avoid the likely risk of the drugs reaching toxic levels (Ramani et al., 2024).

Poly-pharmacy is not always an avoidable event, as in the case of chronic diseases, such as HASeDM, it is necessary to administer numerous drugs to control these pathologies. However, it is essential to underline that these drugs are prescribed appropriately and ensure patient safety. From the study above, the need for health education for the rational use of drugs emerged. Health education can take place through knowledge of possible pharmacological interactions and the development of well-planned actions, which allow us to prevent errors and damage caused to patients, improving the quality of care provided in the healthcare sector (Bullock, 2024; Trolle Lagerros, Grotta, Freyland, Grannas, & Andersson, 2024).

The search for information on the simultaneous use of drugs and herbal medicines, despite being a widespread practice, is not yet consolidated in the population's routine. It has already been

systematically demonstrated that the interaction between drugs and herbal medicines can significantly change the drug profile, resulting in changes in the individual's therapeutic response (Valitabar et al., 2024). Therefore, just as addressing existing drug interactions with conventional medications is essential, it is crucial to evaluate the interaction of herbal medicines. With the indiscriminate use of various drugs, the elderly are highly exposed to side effects and also run the risk of not following the therapy, which could further worsen the disease (Søgaard et al., 2024).

## CONCLUSION:

It is essential to identify potential drug interactions in the treatment of hypertension and diabetes and carry out appropriate therapeutic management to avoid serious adverse effects or even death. The abusive use of drugs, caused by the lack of information on the part of prescribers, dispensers and self-medication, are also factors that lead to reduced effectiveness of treatment and lead to the occurrence of drug interactions. These situations indicate that measures must be adopted to improve the quality of care in the healthcare system, such as continuous training of prescribers and improvement of distribution conditions in these units. The study reveals that older adults are a more vulnerable population to drug interactions. It is necessary to evaluate prescriptions, medical records, and the clinical status of patients to ensure effective and appropriate treatment, avoiding complications that can be avoided thanks to the action of the multidisciplinary team of the health unit. The literature underlines that drug therapy can be deficient even with correct use, since interactions occur, or even because the disease remains silent until it reaches the limit in which the organism is unable to satisfy physiological needs.

Furthermore, this research thoroughly demonstrates the need for more studies, which must be significant and randomized and will attempt to evaluate or clarify diagnosis, treatment, and prevention. It can be combined with older studies as a critical strategy to improve quality of life and more precise protocols, especially in implementing adequate, more detailed and effective management. The studies must be pharmacoepidemiological, especially among patients suffering from chronic diseases, such as hypertension and diabetes mellitus, due to the exacerbated drug use by these individuals in the long term, which also increases the likelihood of drug interactions occurring. One of the study's limitations is linked to the use of a single healthcare unit, which may not contain all the discovered IDs and the small number of patients interviewed. The application of other larger health units will be necessary to confirm and better interpret the data described by the work.

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