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Prevalence and comparative analysis of potential drug-drug interactions among hospitalized patients at a tertiary care cardiac institute in Pakistan: Findings from a single centre

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Abstract: Hospitalized post-operative cardiovascular disease (CVD) patients are often subject to polypharmacy, increasing the risk of potential drug-drug interactions (pDDIs). This observational study assessed 384 post-operative CVD patients for pDDIs using Micromedex Drug-Int® and Lexicomp Interact®. Prevalence, severity, onset, and documentation of pDDIs were analyzed using SPSS 23.0, with logistic regression identifying factors associated with at least two major pDDIs or two pDDIs categorized as X, D, or C. Micromedex Drug-Int® revealed a median of 6.23 pDDIs per patient, with 98.7% of patients having ≥1 pDDIs. Of 2,389 pDDIs, 64.1% were major. Lexicomp Interact® data showed a median of 7.15 pDDIs per patient, with 99.2% of patients having ≥1 pDDIs. Class C interactions were the most frequent (62.1%), followed by Classes B, D, and X. Additionally, the study identified unique pDDIs from Lexicomp, including Ipratropium-Orphenadrine and Furosemide-Levosulpiride, not listed in Micromedex. The findings highlight the high prevalence of pDDIs in this population, emphasizing the need for regular monitoring. Using pDDI screening tools, clinical pharmacists can be crucial in mitigating these risks, particularly in high-risk patients.

Keywords: Potential drug-drug interactions, polypharmacy, CVD, cardiac patient, Micromedex, Lexicomp, Pakistan.

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INTRODUCTION

The World Health Organization states that cardiovascular diseases (CVD) account for 32% of global annual deaths. The majority of these CVD-related deaths, approximately more than three-quarters, are concentrated in low- and middle-income countries (Pandey *et al*., 2023). The prevalence of CVD is estimated to be 17.5% in Pakistan, where 29% of all-cause mortality is due to CVD (Zubair *et al*., 2018). CVD patients are at high risk of potential drug-drug interactions (pDDIs) due to diverse etiologies, multiple comorbidities, and diverse medication regimens (Akbar *et al*., 2021). pDDIs refer to a patient's exposure to a potentially harmful combination of prescribed medications rather than an actual adverse event (Van Leeuwen *et al*., 2013). A pDDI is one of the most preventable drug-related problems that can lead to serious adverse events or treatment failures (Ismail *et al*., 2018). Harmful pDDIs not only compromise therapy but also lead to higher morbidity and mortality rates as well as higher healthcare costs (Murtaza *et al*., 2016). Previous studies have reported a prevalence of pDDIs between 21.3% and 96.9% in CVD patients (Akbar *et al*., 2021). There is consensus within the medical community that pDDIs are predictable and preventable factors that contribute to adverse drug events (ADEs). Therefore, current research and clinical practice guidelines emphasize identifying and preventing pDDIs to mitigate preventable ADEs (Namazi and Moosavi, 2012).

In Pakistan, pDDIs in CVD patients have rarely been studied for their frequency, severity, and risk factors. These studies documented varying prevalence of potential drug-drug interactions (pDDIs), with rates ranging from 42% to 96.5% (Ismail *et al*., 2012, Javaid *et al*., 2017). A study conducted at Ayub Teaching Hospital in Pakistan found that 91.6% of patients with cardiovascular disease (CVD) had at least one pDDI (Murtaza *et al*., 2016). In another prospective observational study, the mean number of pDDIs per patient was 8.50, and all patients (100%) had at least one pDDI screened. The study identified a total of 2787 pDDIs, with 74.06% (n = 2064) classified as moderate severity and 17.33% (n = 483) as major severity (Akbar *et al*., 2021).

Despite their challenging nature and interindividual differences, drug-drug interactions are rarely investigated in clinical studies due to their clinical relevance. To Prevent severe pDDIs and their side effects, drugs that have the lowest risk of pDDIs must be selected (Low *et al*., 2018). It is reported that pDDIs can cause adverse consequences such as hypoglycemia, nephrotoxicity, hyperglycemia, depression of platelet function, increased risk of bleeding, hypokalemia or changes in ECG, and postural hypotension (Khan *et al*., 2017, Mazhar *et al*., 2016, Sankar *et al*., 2015).

To reduce the possibility of pDDIs, a clinical pharmacist should effectively review medication management (Ramalho de Oliveira *et al*., 2010). A computerized drug-

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drug interaction screening tool is vital in such settings, as manual detection and identifying pDDIs is time-consuming and cumbersome. Therefore, interaction tools should be used during prescription and dispensing with active intervention (Moura *et al*., 2012, Taylor and Tamblyn, 2004). Thus, the primary objective of this study was to determine the prevalence, severity levels and risk factors associated with pDDIs among post-operative CVD patients admitted to Pakistan's largest tertiary cardiac care institute.

MATERIALS AND METHODS

Study design and setting

At the National Institute of Cardiovascular Diseases (NICVD), a cross-sectional research study was conducted between November 2021 and April 2022. The study population included only post-operated patients in the surgical ward. The study received approval from the Ethical Review Committee (ERC) of the NICVD under the reference number ERC-117/2021 dated 1st November 2021.

Inclusion and Exclusion Criteria

Patients who received at least two medications (across all routes of administration) and who were at least 18 years old (of both genders) were included in our study. All prescription drugs were given throughout the patient's stay in the hospital. Individuals under the age of 18 were among those who were excluded from the study.

Sample Size & Data Collection

Daniel's sample size calculation formula was used to determine the sample size (Daniel and Cross, 2018, Ismail *et al*., 2013). A total of 384 patients were included in this study. The data collection form is confined to the patient's sociodemographic, clinical and medication information. The patients' medical charts gathered information regarding their primary diagnosis, comorbidities, type of surgery and administered medications. The medications administered to the patients were recorded and listed using their respective generic names.

Data screening

Micromedex Drug-Int.® and Lexicomp Interact® (Abbas *et al*., 2022) were applied for screening pDDIs. With adequate specificity and sensitivity, the IBM Micromedex Drug-Int.® provides reliable scientific evidence regarding potentially interacting drugs (mechanisms of action and adverse outcomes), backed up by the relevant published literature (Kheshti *et al*., 2016). Following the software description, the interactions were categorized into distinct groups based on their severity, onset and levels of documentation.

Levels of severity

Contraindicated: It is contraindicated to use these drugs concurrently.

Major: The potential consequences of this condition can be life-threatening and necessitate medical intervention to minimize or prevent adverse effects.

Moderate: Interactions with other drugs may intensify a patient's symptoms and require adjustments to therapy.

Minor: There would be limited clinical effects from the interaction. The manifestations typically result in an elevated occurrence or heightened severity of adverse effects but do not necessitate substantial modifications in therapy.

Level of documented evidence

Excellent: The interaction has been established by controlled studies.
Good: Despite robust evidence, well-precise studies are lacking.
Fair: Despite the limited documentation available for this interaction, clinical considerations strongly indicate its potential presence or suggest that the available documentation applies to a pharmacologically similar drug.

Level of onset

Rapid: After administration, interactions are observed within 24 hours.
Delayed: After administration, interactions are monitored for more than 24 hours.
Not Specified: The current literature does not provide concrete information on the exact duration of the onset of interaction (Haq *et al*., 2020, Ismail *et al*., 2013).
Lexicomp Interact® is an extensively used, considerate, and specific pDDIs screening tool (Kheshti *et al*., 2016). Lexicomp interact® categorizes each interaction based on its level of need and responsiveness.
A: (no documented interaction)
B: (no further action required)
C: (appropriate therapy monitoring recommended to mitigate undesired outcomes)
D: (Consider therapy modification: To minimize a toxic effect of interaction, appropriate steps must be taken).
X: (avoid combination: Interactions are usually contraindicated since their risks outweigh their benefits) (Akbar *et al*., 2021).

Each patient's list of administered medications was entered into the IBM Micromedex Drug-Int® and Lexi-interact®. A report was generated listing the possible drug-drug interactions with all parameters mentioned above.

STATISTICAL ANALYSIS

A data acquisition Microsoft Excel™ spreadsheet was used to gather the data, which the co-supervisor then examined to ensure it was accurate and comprehensive.

The number of pDDIs for each patient's medication list, interaction classification, risk rating, severity and reliability for each interaction was captured on the MS Excel™ spreadsheet. Using IBM SPSS Statistics Inc.'s Statistical Package for Social Sciences version 23.0, a biostatistician from the clinical research department of NICVD performed a statistical analysis. Chicago, USA). Meanwhile, means, standard deviations, medians and ranges were used to analyze continuous data and frequencies and percentages were used to analyze categorical data. A logistic regression analysis assessed the intercorrelation between different parameters and pDDIs, providing odds ratios (OR) with 95% confidence intervals (CI) for all pDDIs and major pDDIs. Univariate logistic regression analyses were performed using the chi-square test for all variables, considering variables with a p-value of ≤0.1 for assessment in multivariate logistic regression using the Pearson test. A statistically significant threshold of p-value <0.05 was applied in the analysis.

RESULTS

Population Features

Data from 384 CVD patients were collected. The patients in the study had an average age of 48.9 ± 13.9 years. Most patients were male, 70.1%. Among the most common surgeries, 54.2% were Coronary Artery Bypass Grafting (CABG), 15.1% were Mitral Valve Replacements (MVR), and 10.2% were Aortic Valve Replacements (AVR). At least five drugs were prescribed to three patients 0.78%, while 6-7 drugs were prescribed to nineteen patients 4.9%, 8-10 drugs were prescribed to 181 patients 47.1%, and 11 or more medications were noted on 181 patients' prescriptions 47.1% (table 1).

Prevalence and frequency of pDDIs

Based on Micromedex Drug-Int.®, 379 patients (98.7%) had ≥ 1 pDDI in this study. A total of 2389 pDDIs were observed, with a median of 6.23 pDDIs per patient (range 0-20). Of 2389 pDDIs, 64.1% were of major severity, followed by 34.6% moderate, 1.3% minor, and no contraindicated pDDIs. pDDIs pairs with rapid onset of action level were 9.3%, followed by delayed 32% and not specified 58.6%, respectively. The level of documented evidence was excellent 15.5%, followed by 55.3% and 29.2%, respectively. 77% of patients had at least two major pDDIs table 2. Analysis based on Lexicomp, out of 384 patients, 381 patients (99.2%) had ≥1 pDDI. A total of 2739 pDDIs were observed, with a median of 7.15 pDDIs per patient (range 0-26). Based on Lexicomp's risk classification, class C (monitor therapy) was the most common 62.1% class, followed by class B (no action needed), 21.5%, class D (consider therapy modification), 9.5%, and class X (avoid combination), 6.8%. The prevalence of pDDIs in patients with at least two category X, D, or C interactions was 87.8% (table 3).

Table 1: Sociodemographic and baseline characteristics

Variables	Frequency (%)
Gender	
Female	115 (29.9)
Male	269 (70.1)
Age (years)	
Mean ± SD	48.9 ± 13.9
Min - Max	18 - 75
18-30 years	49 (12.8)
31-45 years	81 (21.1)
46-60 years	178 (46.4)
> 60 years	76 (19.8)
Comorbidity	
Yes	272 (70.8)
No	112 (29.2)
Number of comorbidities	
Single	134 (49.3)
Multiple	138 (50.7)
Types of comorbidity	
Hypertension	69 (25.4)
Diabetes mellitus	18 (6.6)
Ischemic Heart Disease	14 (5.1)
Smoking/Tobacco	14 (5.1)
Hypertension and Diabetes mellitus	53 (19.5)
Others	104 (38.2)
Surgery	
CABG	208 (54.2)
MVR	58 (15.1)
AVR	39 (10.2)
Wound Debridement	25 (6.5)
DVR	21 (5.5)
ASD Closure	19 (5.0)
Polypharmacy	
Drugs (Mean ± S.D.)	10.3 ± 1.7
Min - Max	5 - 15
≤5	3 (0.8)
6 to 7	19 (4.9)
8 to 10	181 (47.1)
≥11	181 (47.1)

Potentially interacting drug combinations

Based on the analysis conducted using Micromedex Drug-Int.®, the occurrence of the most prevalent major pDDIs was as follows: 81.5% of patients involved the combination of aspirin and furosemide, 63.8% of patients involved aspirin and amiloride and 52.6% patients involved aspirin and clopidogrel. Drug interaction between aspirin and warfarin accounted for 24.5% of administered drugs (table 4).

From the screening of Lexicomp Interact®, the most frequent pDDIs in category X were clopidogrel and omeprazole 36.5% and ipratropium and orphenadrine 7.6%. The most frequent drug-interacting pair in category D were aspirin and warfarin 24.7% table 5.

Table 2: Summary of pDDIs (Micromedex)

Variables	Frequency (%)
Classification of pDDIs	
Total pDDIs	2389
Min – Max (Mean ± SD)	0 - 20 (6.23 ± 3.02)
Severity	
Major	1532 (64.1)
Moderate	826 (34.6)
Minor	31 (1.3)
Onset	
Rapid	223 (9.3)
Delayed	765 (32.0)
Not Specified	1401 (58.6)
Documented Evidence	
Excellent	370 (15.5)
Good	1321 (55.3)
Fair	698 (29.2)
pDDIs - at least two majors	296 (77.1)
Prevalence of pDDIs (N=384)	
Overall	379 (98.7)
None	5 (1.3)

Table 3: Summary of pDDIs (Lexicomp)

Variables	Frequency (%)
Classification of pDDIs	
Total pDDIs	2739
Min - Max	0 - 26 (7.15 ± 3.67)
Risk rating	
A	2 (0.07)
B	590 (21.5)
C	1702 (62.1)
D	259 (9.5)
X	186 (6.8)
pDDIs - at least two categories X, D, or C	337 (87.8)
Prevalence of pDDIs (N=384)	
Overall	381 (99.2)
None	3 (0.8)

Associated factors for pDDIs

In both univariate and multivariate analyses of Micromedex Drug-Int.®, polypharmacy was significantly associated with pDDIs table 6. Similarly, in both regressions of Lexicomp Interact®, polypharmacy was also significantly related to the occurrence of pDDIs, as shown in table 7.

DISCUSSION

The prevalence and clinical significance of pDDIs in post-operative CVD patients in Pakistan has been a topic of concern due to their possible adverse outcomes and impact on patient safety. This observational study assessed the prevalence of pDDIs and drug-drug interaction screening tools, i.e., Micromedex Drug-Int® and Lexicomp Interact®, in Pakistan's tertiary care cardiac institute.

This research study revealed a superior prevalence of pDDIs among post-operative CVD patients compared to other studies conducted in Pakistan (Akbar, Rehman *et al*., 2021, Ismail, Noor *et al*., 2018). Using Micromedex Drug-Int®, all patients (98.7%) had at least one pDDI, with a mean of 6.23 pDDIs per patient. The majority of pDDIs were of major severity (64.1%), followed by moderate severity (34.6%) and minor severity (1.3%). Comparable results were observed when using Lexicomp Interact®, with 99.2% of patients having at least one pDDI and a median of 7.15 pDDIs per patient. Class C interactions were the most common (62.1%) according to Lexicomp's risk classification. These findings highlight the significant burden of pDDIs among post-operative CVD patients and emphasize the need for effective strategies to mitigate their potential adverse effects. Patients with CVD frequently experience multiple comorbidities, resulting in the utilization of frequent medications beyond cardiac medications. This polypharmacy contributes to a higher prevalence of pDDIs (Humza, 2024, Khan, Sridhar *et al*., 2019).

The study identified various commonly occurring pDDIs. Micromedex analysis revealed that the interaction between aspirin and furosemide was the most frequent major pDDIs (81.5%), followed by aspirin and amiloride (63.8%) and aspirin and clopidogrel (52.6%). Lexicomp Interact® analysis identified the most frequent category X (avoid combination) pDDIs as clopidogrel and omeprazole (35.7%), leading to decreased clopidogrel effectiveness and therapeutic failure. Category D pDDIs are aspirin and warfarin (24.7%). Other notable interactions include ipratropium-orphenadrine (7.6%), causing anticholinergic toxicities, and amiodarone-domperidone (1.6%), causing QT-interval prolongation.

The present study revealed several unique pDDIs classified as category X by Lexicomp Interact® but absent from the Micromedex Drug-Int® database. These interactions include Ipratropium-Orphenadrine, Ipratropium-Potassium Chloride, Orphenadrine-Potassium Chloride, Furosemide-Levosulpride and Orphenadrine-Risperidone. Additionally, the combination of Furosemide and Levosulpride may result in QTc-interval prolongation, posing a significant risk of serious cardiac arrhythmias. Lastly, the Orphenadrine-Risperidone pair could enhance the central nervous system depressant effect, increasing the risk of sedation and other CNS-related side effects.

Table 4: Most frequently identified drug pairs involved in class (major) pDDIs and their potential consequences.

Category	Drug interacting pair	f (%)	Potential consequence
Major	Aspirin - Furosemide	313 (81.5)	Increased risk of salicylate toxicity and reduced diuretic effectiveness
	Aspirin - Amiloride	245 (63.8)	Reduced diuretic effectiveness and hyperkalemia
	Aspirin - Clopidogrel	202 (52.6)	Increased risk of bleeding
	Clopidogrel - Omeprazole	137 (35.7)	Decreased clopidogrel effectiveness and therapeutic failure
	Aspirin - Warfarin	94 (24.5)	Increased risk of bleeding
	Ceftazidime - Warfarin	81 (21.1)	Increased risk of bleeding
	Aspirin - Enoxaparin	77 (20.1)	Increased risk of bleeding
	Enoxaparin - Warfarin	69 (18)	Increased risk of bleeding
	Ciprofloxacin - Domperidone	29 (7.6)	QT- interval prolongation
	Amoxicillin - Warfarin	28 (7.3)	Increased risk of bleeding
	Clopidogrel - Enoxaparin	28 (7.3)	Increased risk of bleeding
	Amlodipine - Clopidogrel	23 (6)	Decreased antiplatelet effect
	Amiloride - Enalapril	20 (5.2)	Hyperkalemia
	Ciprofloxacin - Warfarin	19 (4.9)	Increased risk of bleeding
	Amlodipine - Domperidone	17 (4.4)	QT- interval prolongation
	Aspirin - Digoxin	16 (4.2)	Increased serum concentration of digoxin
	Clopidogrel - Tramadol	12 (3.1)	Reduced efficacy of clopidogrel
	Amiodarone - Warfarin	11 (2.9)	Increased risk of bleeding
	Aspirin - Spironolactone	10 (2.6)	Reduced diuretic effectiveness and hyperkalemia

Table 5: Most frequently identified drug pairs involved in class X and D pDDIs and their potential consequences.

Category	Drug interacting pair	f (%)	Potential consequence
X	Clopidogrel - Omeprazole	137 (35.7)	Decreased clopidogrel effectiveness and therapeutic failure
	Ipratropium - Orphenadrine	29 (7.6)	Anticholinergic related toxicities
	Amiodarone - Domperidone	6 (1.6)	QT- interval prolongation
	Ipratropium - Potassium Chloride	4 (1)	Enhance the ulcerogenic effect of Potassium Chloride
	Diltiazem - Domperidone	1 (0.3)	QT- interval prolongation
	Ipratropium - Quetiapine	1 (0.3)	Anticholinergic related toxicities
	Orphenadrine - Potassium Chloride	1 (0.3)	Enhance the ulcerogenic effect of Potassium Chloride
	Enoxaparin - Rivaroxaban	1 (0.3)	Increased risk of bleeding
	Furosemide - Levosulpride	1 (0.3)	QT- interval prolongation
	Domperidone - Verapamil	1 (0.3)	Increase the serum concentration of domperidone
	Orphenadrine - Risperidone	1 (0.3)	Enhance the CNS depressant effect of orphenadrine
D	Aspirin - Warfarin	95 (24.7)	Increased risk of bleeding
	Aspirin - Enoxaparin	89 (23.2)	Increased risk of bleeding
	Clopidogrel - Enoxaparin	30 (7.8)	Increased risk of bleeding
	Amiodarone - Warfarin	11 (2.9)	Increased risk of bleeding
	Amiloride - Potassium chloride	6 (1.6)	Hyperkalemia
	Aspirin -Rivaroxaban	5 (1.3)	Increased risk of bleeding
	Domperidone - Quetiapine	3 (0.8)	QT- interval prolongation
	Amiodarone - Digoxin	2 (0.5)	Increase the serum concentration of digoxin

Table 6: Micromedex Drug Interaction - at least two majors

	Univariate		Multivariable	
	OR [95% CI]	P-value	OR [95% CI]	P-value
Male	1.78 [1.08 -2.93]	0.023	1.68 [0.89 -3.18]	0.109
Age ≥ 65 years	1.25 [0.62 -2.54]	0.529	-	-
Hypertension	1.49 [0.91 -2.43]	0.113	1.42 [0.71 -2.83]	0.321
Diabetes Mellitus	1.89 [0.77 -4.65]	0.164	3.57 [1.08 -11.77]	0.037
Smoking	0.58 [0.21 -1.59]	0.287	-	-
Ischemic Heart Disease	0.64 [0.22 -1.9]	0.421	-	-
CABG	2.13 [1.31 -3.46]	0.002	1.18 [0.54 -2.58]	0.682
MVR	1.44 [0.69 -2.98]	0.332	-	-
AVR	0.92 [0.4 -2.12]	0.850	-	-
DVR	2.95 [0.67 -12.92]	0.151	3.91 [0.75 -20.37]	0.106
Total number of drugs	2.11 [1.74 -2.55]	<0.001	2.21 [1.78 -2.75]	<0.001

Table 7: Lexicomp Drug Interaction - at least two categories X, D, or C

	Univariate		Multivariable	
	OR [95% CI]	P-value	OR [95% CI]	P-value
Male	2.82 [1.52 -5.25]	0.001	2.89 [1.39 -6.04]	0.005
Age ≥ 65 years	1.19 [0.48 -2.95]	0.707	-	-
Weight	1.02 [1 -1.04]	0.062	1 [0.97 -1.03]	0.962
Hypertension	1.06 [0.57 -1.96]	0.860	-	-
Diabetes Mellitus	1.92 [0.57 -6.48]	0.293	-	-
Smoking	1.12 [0.25 -5.04]	0.881	-	-
Ischemic Heart Disease	2.14 [0.28 -16.61]	0.466	-	-
CABG	2.31 [1.23 -4.35]	0.01	0.93 [0.4 -2.17]	0.867
AVR	2.28 [0.53 -9.85]	0.270	-	-
Total number of drugs	1.83 [1.5 -2.24]	<0.001	1.88 [1.5 -2.36]	<0.001

These findings underscore the importance of cross-referencing multiple drug interaction databases to ensure comprehensive identification of potential drug interactions, as relying on a single source may overlook critical pDDIs.

These findings provide insight into specific drug combinations that pose a higher interaction risk among post-operative CVD patients, enabling healthcare professionals, especially clinical pharmacists, to prioritize their attention and respond appropriately to minimize potential harm. Nevertheless, electronic databases serve as valuable tools for identifying pDDIs and can aid in making informed clinical decisions, including adjusting the treatment regimen or discontinuing drug pairs that exhibit interactions (Shakeel *et al*., 2018).

Our study identified that most patients frequently used QTc-interval prolonging medications, which may increase the risk of QTc-interval prolongation (Humza *et al*., 2024). It is recommended that pharmacists become more educated and aware of QTc-interval prolongation when conducting drug reviews. Pharmacist-driven QTc-interval monitoring must be implemented to decrease the risk of QTc-interval prolongation (Humza *et al*., 2022).

Polypharmacy and male gender were identified as significant risk factors associated with pDDIs. Patients receiving multiple drugs (polypharmacy) were more likely to experience pDDIs, consistent with previous studies highlighting the increased risk of interactions with a higher number of medications (Humza 2024, Khezrian *et al*., 2020, Kim *et al*., 2014). The association between male gender and pDDIs suggests that gender-specific factors, such as differences in drug metabolism and pharmacokinetics, may contribute to the susceptibility to interactions. These findings emphasize the importance of considering these risk factors during medication management and monitoring to reduce the occurrence of pDDIs among post-operative CVD patients (Diksis, *et al*., 2019, Murtaza *et al*., 2016).

The role of clinical pharmacists is crucial to manage and monitor patients with pDDIs effectively. Clinical pharmacists possess the expertise to evaluate medication regimens, identify potential interactions, and provide recommendations for appropriate management (Ahmed *et al*., 2021). Computer-based drug-drug interaction screening tools, such as Micromedex Drug-Int® and Lexicomp Interact®, are vital in supporting pharmacists in detecting pDDIs. Pharmacists should enhance their knowledge of potential drug-drug interactions (pDDIs)

and collaborate to develop educational programs. These initiatives aim to improve patient counseling and minimize the improper use of medications. We strongly advise prioritizing a thorough evaluation of the patient's medication list before determining the desirability or undesirability of a specific drug combination to mitigate potential drug interactions.

The study population was limited to post-operative patients in a specific surgical ward at the NICVD. This specialized setting may not fully represent the broader CVD population, potentially introducing selection bias. Patients in different settings or with different health conditions might exhibit different patterns of medication use and pDDIs (Rodriguez-Gonzalez *et al*., 2012). The study was conducted in a single tertiary care centre in Pakistan, so the findings may not be generalizable to other areas or healthcare settings with different patient demographics or healthcare practices. Variations in drug prescribing practices, availability, and patient management strategies across different settings could influence the prevalence and nature of pDDIs (Ismail *et al*., 2018). The study used Micromedex Drug-Int.® and Lexicomp Interact® for screening pDDIs. While these tools are widely used and provide valuable insights, they have limitations. Variations in drug interaction classifications and updates may affect the consistency and completeness of the findings (Akbar *et al*., 2021; Haq *et al*., 2020). These limitations highlight the need for caution in interpreting the study results and suggest that further research with longitudinal designs, broader patient populations, and updated interaction databases may provide more comprehensive insights into the impact of pDDIs on patient safety.

CONCLUSION

Considerable numbers of patients with post-operative CVD are exposed to pDDIs. Major pDDIs and category X or D are of particular concern. In both univariate and multivariate analyses of Micromedex Drug-Int.® and Lexicomp Interact®, polypharmacy was significantly associated with pDDIs. Clinical pharmacist can play a vital role in identifying and preventing pDDIs and computer-based screening tools for pDDIs can support their efforts in a time-efficient way.

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