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Medication Errors and Drug Therapy Related Problems in Hypertensive Cardiovascular Patients: A Prospective Evaluation Using the PCNE Classification in a Critical Care Setting

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Abstract

Introduction: Medicines are essential in modern healthcare, contributing to the prevention, diagnosis, and management of disease. When misused, however, they may lead to drug therapy–related problems (DTRPs) such as medication errors and adverse drug reactions. Critically ill patients with cardiovascular disease and hypertension are particularly vulnerable because of complex treatment regimens. Although international studies highlight the role of clinical pharmacists in reducing such problems, their participation in patient care remains limited in Pakistan. This study applied the Pharmaceutical Care Network Europe (PCNE) classification system (v9.1) to assess DTRPs among hypertensive patients in a critical care setting. Objective: To identify and classify DTRPs using the PCNE system (v9.1) among hypertensive cardiovascular patients admitted to the Critical Care Unit (CCU) of DHQ Hospital Kohat, and to evaluate the contribution of clinical pharmacists in addressing these problems. Methods: This prospective observational study was carried out over six months (December 2024–May 2025). Adult inpatients (>18 years) diagnosed with cardiovascular disease and hypertension were included. From 180 patient records, 100 were selected according to inclusion criteria. Data on demographics, clinical conditions, and treatments were collected using structured forms. DTRPs were identified and classified using Micromedex, Lexicomp, Medscape, and standard clinical references. Data analysis was performed with Microsoft Excel and SPSS version 16.0. Results: A total of 463 DTRPs were identified, with a mean of 4.77 per patient. The most frequent categories were suboptimal therapeutic effect (32.18%), potential adverse drug events (28.29%), and prescriptions without clear indication (19.65%). Inappropriate drug combinations represented 12.95% of cases. The most common interventions involved drug withdrawal or dose adjustment (25.05%) and control of antibiotic use (21.59%). Higher age and multiple comorbidities were significantly associated with increased frequency of DTRPs. Conclusion: The study shows a considerable burden of preventable DTRPs among hypertensive cardiovascular patients in the CCU. Clinical pharmacist involvement was effective in resolving many of these problems. Strengthening the role of pharmacists within multidisciplinary teams

can improve therapeutic outcomes and enhance medication safety in public sector hospitals.

1. INTRODUCTION

Medications are an indispensable part of modern healthcare systems, widely used for the prevention, diagnosis, and treatment of disease across diverse clinical settings. When prescribed and monitored appropriately, they improve therapeutic outcomes, delay disease progression, and enhance patients' quality of life. At the same time, inappropriate use or insufficient monitoring can lead to harmful consequences, often linked to pharmacokinetic or pharmacodynamic issues [1]. A major concern in this regard is drug therapy–related problems (DTRPs), defined as any event associated with drug therapy that prevents or potentially prevents desired health outcomes.

DTRPs represent a broad spectrum of medication issues, including adverse ADRs, medication errors, suboptimal drug selection, incorrect dosing, drug–drug interactions, and poor adherence. Such problems are clinically important because they can lead to therapeutic failure, prolonged hospital stays, higher healthcare costs, and in severe cases, morbidity and mortality. The risk is especially pronounced among hospitalized patients, where complex regimens and polypharmacy greatly increase the chance of errors.

Critically ill patients admitted to intensive or critical care units face even greater vulnerability. Most present with severe cardiovascular conditions and frequently require multiple medications to manage comorbidities such as hypertension, diabetes, or renal dysfunction. In these settings, high-alert medications like anticoagulants, inotropes, and antiarrhythmics often with narrow therapeutic windows are used on a routine basis. As a result, even seemingly minor prescribing or administration errors can escalate into serious or life-threatening outcomes [2].

Evidence from developed healthcare systems demonstrates that clinical pharmacists, when embedded in multidisciplinary teams, play a central role in mitigating these risks. Their responsibilities extend beyond dispensing; they monitor drug therapy, adjust treatment regimens, detect existing or potential DTRPs, and promote safer, evidence-based care [1,2]. Countries such as the United States, the United Kingdom, and several in Europe have shown that their involvement reduces prescribing errors, strengthens compliance with treatment guidelines, and improves overall patient safety.

In contrast, in Pakistan the contribution of clinical pharmacists in direct patient care remains limited, particularly in the public sector. Their role is largely confined to dispensing activities [3], despite strong international and national recommendations advocating their inclusion in clinical decision-making [4]. This underutilization stems from multiple barriers, including lack of awareness among medical staff, institutional constraints, and professional resistance. Furthermore, there is very little local research documenting the prevalence, classification, and impact of DTRPs, especially in critical care settings [5]. In provinces such as Khyber Pakhtunkhwa, where patient loads are high and resources are limited, data on medication-related problems remain scarce [6,7].

To fill this gap, the present study was carried out in the Critical Care Unit of DHQ Hospital Kohat, a major referral center for southern Khyber Pakhtunkhwa. The study assessed the prevalence, nature, and contributing factors of DTRPs in hypertensive patients, with a focus on identifying strategies to minimize such problems [8]. For this purpose, the Pharmaceutical Care Network Europe (PCNE) classification system, version 9.1, was applied. The PCNE framework provides a standardized method to categorize problems, their causes, pharmacist interventions, and outcomes, thereby enabling meaningful comparisons with international evidence [9–11].

By generating local data, this work aims to highlight the scale and nature of DTRPs in a critical care setting, underscore the importance of clinical pharmacists in tertiary care hospitals, and guide policy-level efforts to expand their role in multidisciplinary teams. Ultimately, the findings contribute to global health priorities on medication safety, rational use of medicines, and collaborative models of care, while providing much-needed evidence from Pakistan [12].

2. METHODOLOGY

2.1 Study Design: The study design was Prospective-observational study involved cardiovascular patients admitted to the CCU ward at DHQ Hospital Kohat, a 450-bed tertiary care teaching facility in Kohat, Khyber Pakhtunkhwa, Pakistan, and was carried out over a six-month period (December 2024 to May 2025).

2.2 Study Population: During the specified reference period, clinical history information for 180 patients was collected using the WHO sample size calculator, and 100 patients who met the study's inclusion requirements were chosen to take part.

2.3 Inclusion and Exclusion Criteria: The study included adult patients aged over 18 years, of either gender, who were admitted to the Critical Care Unit (CCU), provided informed consent, and had a confirmed diagnosis of hypertension along with a cardiovascular illness. Patients were excluded if they were managed on an outpatient basis, were pregnant, belonged to the pediatric age group, lacked a confirmed diagnosis of hypertension, had multiple complications referred from other hospital wards, or declined to participate in the study.

2.4 Data Collection Procedure: During the study period, patient histories were obtained from a total of 180 individuals, out of which 100 medication orders were

selected for analysis according to the predefined inclusion criteria. The collected information was systematically documented using a structured data collection form, which included details on patient demographics, reasons for hospital admission, past medical and medication histories, as well as disease-specific information.

2.5 Data Interpretation: Following the evaluation and interpretation of the collected data, DTRPs were identified and assessed utilizing resources such as Micromedex, Lexi comp, Medscape, and other clinical guidelines [13, 14]. Appropriate clinical interventions were then suggested for prescribers, and the DTRPs were categorized using the (PCNE) version 9.1 classification system. The results were plotted following the suitable statistical analysis tests utilizing Microsoft Excel and SPSS version 16.0.

2.6 Ethical Approval: Approval for this observational study was obtained from the Institutional Ethics Committee of Kohat University of Science and Technology (KUST). Informed consent was obtained from all patients prior to data collection, and the study was conducted in full compliance with established ethical guidelines.

3. RESULTS

The study included 100 hypertensive patients, and a total of 463 DTRPs were identified, averaging 4.77 problems per patient. This reflects a considerable burden of medication-related challenges in the study group. Most patients were older adults, with 71.13% aged 60 years or above, highlighting the well-known association between age and cardiovascular disease. Males accounted for 55.67% of the participants, while 62.88% had one or two comorbid conditions in addition to hypertension. Polypharmacy was common, as more than half of the patients (50.51%) were prescribed between 6 and 10 medications. Moreover, 67.01% of patients had blood pressure readings in the high-normal range, indicating suboptimal control despite treatment. These patterns suggest that advancing

age, multiple comorbidities, and extensive drug use collectively increased the likelihood of DTRPs in this population.

TABLE 1: *HEALTH INFORMATION AND DEMOGRAPHICS OF THE PATIENT POPULATION*

Variable	Frequency (n=100) (%)
GENDER	
Male	54(55.67%)
Female	43(44.32%)
AGE (Years)	
<30	0
30-39	3(3.09%)
40-49	13(13.40%)
50-59	12(12.37%)
60 & above	69(71.13%)
CO MORBIDITIES	
Nil	10(10.30%)
1-2	61(62.88%)
>3	26(26.80%)
NUMBER OF DRUGS	
1-5	8(8.24%)
6-10	49(50.51%)
>10	40(41.23%)
HYPERTENSION TYPE	
High Normal	65(67.01%)

The distribution of the 463 DTRPs is depicted in Figure 1. The most frequently reported

categories included adverse drug reactions (ADRs), therapeutic duplication, inadequate therapy, and inappropriate drug selection. This distribution suggests that both safety-related and efficacy-related issues were widespread. The presence of therapeutic duplication and inappropriate selections highlights lapses in rational prescribing practices, while inadequate therapy points toward under-treatment or omission of essential drugs.

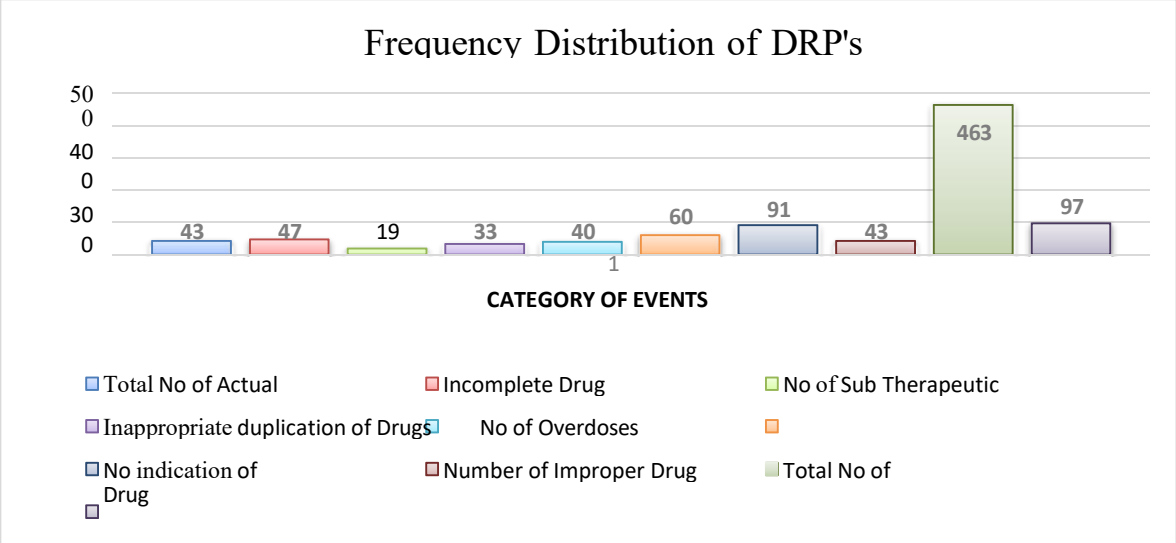

Figure 1. Distribution of Drug-Related Problem Subtypes by Frequency. The most and least frequent categories found in the study are highlighted in this graph, which shows the frequency of each subtype of drug-related issues found among the patients.

Using the PCNE classification system (v9.1), the DTRPs were grouped into categories of treatment efficacy, treatment safety, and other associated problems (Table 2). Almost half of the cases (46.22%) were related to insufficient treatment success, as reflected by unresolved or poorly managed symptoms. Treatment safety issues, such as ADRs and the risk of drug toxicity, were reported in 25.48% of cases. These data demonstrate that both under-treatment and unsafe treatment contribute substantially to poor clinical outcomes.

TABLE 2: *PROBLEMS ASSOCIATED WITH SUBSTANCE-RELATED ISSUES BASED ON PCNE SCALE SYSTEM VERSION 9.1 FOR CATEGORIZATION*

CODE	Detailed Classification	n (%)
P1	Treatment Effectiveness	214(46.22%)
P1.1	No effect of drug treatment despite correct use	51(11.01%)
P1.2	Effect of drug treatment not optimal	149(32.18%)
P1.3	Untreated symptoms or indication	14(3.02%)
P2	Treatment safety	118(25.48%)
P2.1	Adverse drug event (possibly) occurring	
P3	Other	131(28.29%)
P3.1	Unnecessary drug treatment	95(20.51%)
P3.2	Unclear problem/complaint. Further clarification necessary	36(7.77%)

The causes of DTRPs, based on PCNE sub-classification, are detailed in Table 3. The leading contributor was inappropriate drug selection (61.12%), which included irrational combinations, therapeutic duplication, and failure to prescribe guideline-directed therapy. Dose-related problems, such as inaccurate dosing frequency or inappropriate instructions, were also common. Additional contributors included inappropriate treatment durations, dispensing errors, and patient-related factors such as misunderstanding instructions or non-adherence. These findings emphasize that DTRPs are multifactorial in origin, with prescriber decisions, healthcare system gaps, and patient behaviors all playing a role.

TABLE 3: *FOUND FACTORS USING THE PCNE SCALE SYSTEM VERSION 9.1FOR CATEGORIZING TO CAUSES RELATED TO ISSUES IN DRUG THERAPY PRESCRIBED*

PCNE CODE	Detailed Classification	n (%)
C1	Selection of Drug	283(61.12%)
C1.1	Unsuitable drug selection according to guidelines/formulary	43(9.28%)
C1.2	No indication for drug selected	91(19.65%)
C1.3	Unsuitable combination of drugs, or drugs and herbal medications, or drugs and dietary supplements being prescribed	60(12.95%)
C1.4	Unsuitable therapeutic duplication of group or active ingredient	33(7.12%)
C1.5	No or incomplete drug treatment in spite of existing indication	47(10.15%)
C1.6	Too many different drugs/active ingredients prescribed for indication	9(1.94%)
C2	Form of the Drug	21(4.53%)
C2.1	Inappropriate form/formulation of drug (for this patient)	21
C3	Selection of Dose	72(15.55%)
C3.1	Dose of Drug too low	19(4.10%)
C3.2	Dose of a drug single active ingredient too high	40(8.63%)
C3.3	Dosage regimen not frequent enough	4(0.86%)
C3.4	Dosage regimen too frequent	5(1.07%)

C3.5	Dose timing instructions wrong, unclear or missing	4(0.86%)
C4	Treatment Duration	08(1.72%)
C4.1	Treatment Duration too short	3(0.64%)
C4.2	Treatment Duration too long	5(1.07%)
C5	Dispensing	9(1.94%)
C5.2	Necessary information not provided or incorrect advice provided	9
C6	Drug use Process	10(2.15%)
C6.1	Inappropriate timing of administration or dosing intervals by a health professional	3(0.64%)
C6.5	Wrong drug administered by a health professional	1(0.215%)
C6.6	Drug administered via wrong route by a health professional	6(1.29%)
C7	Patient Related	9(1.94%)
C7.1	Patient intentionally uses/takes less drug than prescribed or does not take the drug at all for whatever reason	4(0.86%)
C7.10	Patient unable to understand instructions properly	5(1.07%)
C9	Other	51(11.01%)
C9.1	No or inappropriate outcome monitoring (incl TDM)	30(6.47%)
C9.2	Other cause, specify	21(4.53%)

Pharmacist-led interventions undertaken to address the identified DTRPs are summarized in Table 4. The majority of interventions occurred at the prescriber level (55.29%), such as recommending drug initiation, withdrawal, or adjustment of therapy. Drug-level

interventions (19.87%) included dose modification and discontinuation of inappropriate agents. Patient-level interventions (12.74%) consisted primarily of counseling and engaging caregivers to improve adherence and understanding of therapy. These data strongly support the clinical relevance of pharmacist involvement in multidisciplinary healthcare teams to optimize therapeutic outcomes.

TABLE 4: *REGULARITY OF CLINICAL INTERVENTIONS OR RECOMMENDATIONS TO PHYSICIANS FROM PHARMACISTS*

PCNE CODE	Types of Recommendation	Total
I0	NO Intervention	0
I1	At prescriber level	256(55.29%)
I1.1	Prescriber informed only (cessation of antibiotics used)	100(21.59%)
I1.2	Prescriber asked for information	14(3.02%)
I1.3	Intervention proposed to prescriber (Add necessary drugs and discontinue unwanted drugs as per standard treatment guidelines)	116(25.05%)
I1.4	Intervention discussed with prescriber	26(5.61%)
I2	At Patient level	59(12.74%)
I2.1	Patient (Drug) Counselling	51(11.01%)
I2.2	Written information provided only	5(1.07%)
I2.4	Spoken to family member/caregiver	3(0.64%)
I3	At Drug Level	92(19.87%)
I3.1	Drug changed to	17(3.67%)
I3.2	Dosage changed to	18(3.88%)

I3.4	Instructions for use changed to	4(0.86%)
I3.5	Drug Paused or stopped	47(10.15%)
I3.6	Drug started	6(1.29%)
I4	Other	56(12.09%)
I4.1	Other intervention	52(11.23%)
I4.2	Side effects reported to authorities	4(0.86%)

The associations between patient-related factors and DTRP frequency were statistically significant. As presented in Table 5, polypharmacy was strongly correlated with DTRPs, with patients prescribed >10 medications contributing to 233 DTRPs, compared to far fewer in those prescribed ⩽5 medications (χ^2 = 136.612, p < 0.001). Similarly, Table 6 demonstrates that patients with >3 comorbidities accounted for 291 DTRPs, compared to substantially fewer in those with ⩽2 comorbidities (χ^2 = 200.246, p < 0.001). Finally, Table 7 highlights the impact of age, with patients ⩾60 years reporting 330 DTRPs, a significantly higher burden compared to younger age groups (χ^2 = 540.793, p < 0.001). These results reinforce the established associations of polypharmacy, multimorbidity, and older age with higher risks of medication-related problems.

A strong correlation was observed between the number of medications prescribed and the occurrence of DRPs (Table 5). Patients receiving more than ten medications experienced the highest burden of DRPs (n = 233), compared with those on 6–10 drugs (n = 190) or 1–5 drugs (n = 38). The association between polypharmacy and DRP frequency was highly significant (χ^2 = 136.612, df = 2, p < 0.001).

TABLE 5: *CROSS-TABULATION OF THE OCCURRENCE OF DRP'S AMONG PATIENTS AND THE NUMBER OF MEDICATIONS ADMINISTERED*

Number of Medications	Observed Frequency	Expected Frequency	Residual	χ^2 Value
Occurrence of DRPs	Observed Frequency	Expected Frequency	Residual	χ^2 Value
1–5	38	153.7	-115.7	
6–10	190	153.7	36.3	
>10	233	153.7	79.3	
Total	461			χ^2 = 136.612 df = 2 p<0.001

Similarly, the frequency of DRPs increased with the number of comorbidities (Table 6). Patients with more than three comorbid conditions accounted for the majority of DRPs (n = 291), compared with those having 1–2 comorbidities (n = 124) or none (n = 48). The correlation between comorbidity burden and DRP occurrence was statistically significant (χ^2 = 200.246, df = 2, p < 0.001).

TABLE 6: *CO RELATION BETWEEN THE FREQUENCY OF DRP'S AND PATIENT COMORBIDITIES*

Number of Co-morbidities	Observed Frequency	Expected Frequency	Residual	χ^2 Value
Nil	48	154.3	-106.4	
1-2	124	154.3	-30.3	
>3	291	154.3	136.7	

Total	463	χ^2 = 200.246 df = 2 p<0.001

Age was also strongly associated with DRP frequency (Table 7). Patients aged >60 years reported the highest number of DRPs (n = 330), while those in younger age groups (30–39 years, n = 14; 40–49 years, n = 57; 50–59 years, n = 62) experienced significantly fewer. This relationship was highly significant (χ^2 = 540.793, df = 3, p < 0.001), indicating that older patients are particularly vulnerable to medication-related problems.

TABLE 7: *THE CO-RELATION LINKAGE AMONG THE NUMBER OF REPORTED DRP'S WITH THE PATIENT'S AGE*

Age Groups(Years)	Observed Frequency	Expected Frequency	Residual	χ^2 value
30-39	14	115.8	-101.8	
40-49	57	115.8	-58.8	
50-59	62	115.8	-53.8	
>60	330	115.8	214.2	
Total	463		χ^2=540.793 df=3 P<0.001	

4. DISCUSSION

DTRPs are recognized as important contributors to compromised patient safety, therapeutic failure, increased hospitalizations, and higher healthcare costs [15]. In this study, a systematic approach was used to identify, classify, and quantify DTRPs among hypertensive patients in a critical care setting. The findings highlight both the extent of the problem and the need for systematic interventions to optimize patient care.

In this study, an average of 4.77 drug therapy–related problems (DTRPs) were identified per patient, a figure considerably higher than earlier reports using the PCNE system, which documented mean values of 1.5 [15], 2.2 [2], and 1.675 [16]. The variation may be explained by differences in study design, patient mix, or prescribing practices. Nonetheless, the higher frequency observed here points to the need for closer prescription oversight and stronger compliance with evidence-based protocols in the local setting.

Age was a major determinant of DTRP occurrence. Patients aged 60 years and older accounted for over 70% of all cases, a finding consistent with previous studies linking older age to multimorbidity, altered drug metabolism, and a higher risk of adverse events [17,18]. Polypharmacy further compounded this risk: more than half of the DTRPs were found in patients taking between six and ten medications. This relationship between increasing drug count and higher DTRP burden has been documented in earlier research as well [19]. These observations reinforce the importance of systematic medication reconciliation and careful review of prescriptions in elderly and high-risk groups.

The study also revealed substantial prescribing gaps. Almost one in five DTRPs involved the use of medications without clear therapeutic indications, while nearly 13% reflected omission of therapies supported by evidence. For instance, patients with heart failure with reduced ejection fraction (HFrEF) were often not prescribed standard regimens such as ACE inhibitors/ARNIs, beta-blockers, MRAs, or SGLT2 inhibitors, despite strong guideline recommendations from the 2021 European Society of Cardiology [20]. These agents are well established to reduce morbidity, mortality, and hospital readmissions [21]. Their underuse suggests deficiencies in adherence to international treatment standards. In addition, drug–drug and drug–supplement interactions (12.95%) were frequent,

emphasizing the importance of thorough medication histories and structured reviews. Interventions by pharmacists proved valuable in resolving identified problems. Prescriber-level recommendations most often involving initiation or discontinuation of therapy—accounted for about a quarter of interventions. Adjustments in antibiotic therapy represented another significant portion (21.5%), reflecting the need for stewardship in antimicrobial use. Patient-level actions, including counseling, were less common but still contributed meaningfully to safer therapy. These findings align with global evidence that pharmacist participation reduces prescribing errors, optimizes treatment, and eases the burden on health systems [23].

Statistical analyses confirmed significant associations between DTRPs and factors such as advanced age, polypharmacy, and multimorbidity, in line with earlier studies [24,25]. Patients with complex drug regimens and multiple comorbidities are at particularly high risk, highlighting the need for multidisciplinary management strategies. Regular prescription audits, guideline-directed therapy, and active pharmacist involvement are among the most effective measures to minimize such risks.

In summary, this study underscores the urgent need for structured systems to monitor and manage DTRPs in critical care. Multidisciplinary collaboration, with clinical pharmacists playing an active role, offers a practical approach to reducing medication-related harm, improving patient outcomes, and alleviating both clinical and economic pressures on healthcare services.

5. CONCLUSION

In this study, DTRPs were found to be frequent among hypertensive patients in critical care. These problems interfere with treatment goals, threaten patient safety, and add to the cost and complexity of care. Of note, older patients, those with multiple illnesses,

and those exposed to polypharmacy were particularly vulnerable. The findings suggest that clinical pharmacists can make a meaningful difference by reviewing prescriptions, identifying therapy-related risks, and guiding adjustments when necessary. Their participation not only supports safer and more rational medicine use but also encourages adherence and reduces preventable harm. Moving forward, the integration of pharmacists as active members of the healthcare team should be prioritized to improve patient outcomes and reduce the burden on the health system.

LIMITATIONS

This study was limited to a single critical care setting, which may restrict generalizability. Being observational, it relied on available records and the PCNE classification system, leaving room for underreporting or misclassification of DRPs. The focus on hypertensive patients and the modest sample size may not represent the broader patient population. Additionally, confounding factors such as prescriber practices and medication availability were not controlled, and long-term patient outcomes were not assessed.

CONFLICT OF INTEREST

The authors of the manuscript have no financial or non-financial conflict of interest in this research manuscript.

DATA AVAILABILITY

Relevant data generated and analyzed during this study can be obtained from the corresponding author upon request. Access to certain portions of the dataset may be limited in order to maintain patient confidentiality and comply with institutional guidelines.

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