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Potential Drug-Drug Interactions among Chronic Heart Failure Patients Managed at Lagos University Teaching Hospital, Nigeria

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ABSTRACT

With increasing life expectancy among chronic heart failure (CHF) patients, particularly the elderly, polypharmacy has become common due to multiple coexisting conditions. This significantly elevates the risk of drug-drug interactions (DDIs), which pose a major challenge to patient safety and highlight the need for improved healthcare delivery strategies. A descriptive cross-sectional study was conducted among 110 CHF patients at Lagos University Teaching Hospital (LUTH). Data were collected using a pre-tested, interviewer-administered questionnaire. Information on medications prescribed at admission and discharge was extracted from patient case notes and discharge summaries. Potential DDIs were assessed using Lexi-Interact™ software, and data were analyzed using SPSS. Odds ratios (ORs) with 95% confidence intervals (CIs) were computed, and p-values less than 0.05 were considered statistically significant. Of the 110 participants, 49 (44.5%) were male and 61 (55.5%) female, with an age range of 40–90 years and a mean age of 62.14 ± 10.24 years. Marital status distribution showed 66.4% were married, while 27.3% were widowed. Over half (53.6%) were employed, and the majority (69.1%) had completed secondary education. The most frequently prescribed medications were clopidogrel and furosemide (31.8% each), followed by losartan (28.2%), digoxin, and lisinopril (24.5% each). A total of 109 patients (99.1%) were on more than one medication, with a mean of 3.92 ± 1.60 drugs per patient. More than half (52.6%) were either overweight or obese. The overall prevalence of potential DDIs was 70.9% (78 patients). Significant associations were found between potential DDIs and length of hospital stay ($p < 0.001$), systolic blood pressure ($p < 0.001$), diastolic blood pressure ($p = 0.026$), and heart rate ($p < 0.000$). This study reveals a high prevalence of potential DDIs among CHF patients. Clinicians are strongly encouraged to utilize clinical decision support tools or DDI-checking software when prescribing medications. Polypharmacy and comorbidities remain key contributors to adverse drug events, which increase treatment costs, prolong hospital stays, and compromise patient safety. Evidence-based and innovative strategies are urgently needed to mitigate these risks and enhance medication safety in this vulnerable population.

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Key Words
Prevalence, potential drug-drug interactions, chronic heart failure

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INTRODUCTION

The life expectancy of patients with chronic heart failure (CHF) is improving due to the widespread use of medications. However, most of these patients are elderly and often have multiple comorbid conditions that necessitate polypharmacy, thereby increasing the likelihood of drug-drug interactions (DDIs)[1]. Ensuring the safety of these patients has become an important challenge and a significant opportunity for stakeholders to enhance healthcare outcomes[1].

Over recent decades, both the public and the medical community have increasingly focused on medication errors (MEs) and adverse drug events (ADEs) due to their serious implications for public health and safety. For example, in Iran, approximately 98,000 deaths occur annually in hospitals due to MEs, while in the United States, drug-related morbidity and mortality cost around $76.6 billion each year[2]. In contrast, sub-Saharan Africa has limited data regarding potential drug-drug interactions (PDDIs). ADEs are often the result of PDDIs, which are generally preventable. Thus, to reduce the incidence of ADEs, interventions are needed for PDDIs-these include dose modifications, substituting safer alternatives, and monitoring for clinical signs and symptoms by healthcare professionals[1].

DDIs are described as the interaction between two or more medications that alters the efficacy or toxicity of one or more of them[1,3]. Another definition sees DDIs as changes in therapeutic effect or adverse outcomes when drugs are taken together[4]. These interactions contribute significantly to ADEs, emergency department visits, hospital admissions, and readmissions[4]. As a consequence, DDIs increase hospitalization durations and healthcare expenditures[4]. Therefore, managing PDDIs is vital to improving medication safety.

As a distinct category of adverse drug reactions, DDIs present a major obstacle in managing chronic heart failure, particularly since many CHF patients are elderly, often on multiple medications, and commonly have coexisting health conditions alongside declining organ function.

The likelihood of PDDIs rises with the number of medications, extended hospital stays, and the presence of comorbidities[5]. A study in Nepal identified a 21.3% incidence rate of potential DDIs and 48 interactions considered hazardous[5]. The most frequent drug pairs involved were enalapril/metformin (10.4%), atorvastatin/ azithromycin (10.4%), enalapril/potassium chloride (10.4%), atorvastatin/clarithromycin (8.3%), and furosemide/gentamicin (6.3%). Commonly implicated drugs included enalapril, atorvastatin, digoxin, clopidogrel, furosemide, and warfarin[5]. Most interactions were of moderate severity and pharmacokinetic in nature (62.5%)[5].

Research across various contexts confirms that DDIs are a widespread issue. An Iranian study showed that potential DDIs were common among outpatients on multiple medications, with the rate correlating with the number of drugs prescribed[1]. In a U.S. study involving over 30,000 Medicare patients in ambulatory care, 1,523 ADEs were identified in one year, with 24.6% deemed preventable and 38% classified as life-threatening or fatal. The incidence rate was 50.1 ADEs per 1,000 person-years, with 13.8 of those being preventable[1]. Similarly, in Italy, among 16,037 patients visited by general practitioners, 895 potential DDIs were identified. Of these, 119 distinct severe PDDIs occurred 1,037 times in 758 patients-representing 4.7% of all patients. Most (74%) had only one DDI, but six patients (0.04%) had five different PDDIs[1]. In the U.S., 2.3% of adults in a health maintenance organization had a potential DDI.

An Ethiopian study reported a 72.2% overall prevalence of PDDIs (95% CI: 59.1–85.3%), with major, moderate, and minor interactions occurring at rates of 25.1%, 52.8%, and 16.9%, respectively, and 1.27% being unclassified[6]. The frequency of DDIs rises sharply when more drugs are prescribed-ranging from 13% with two drugs to 81% with more[7]. This trend is especially pronounced in chronic heart failure patients, where polypharmacy is common[7].

In the U.S., the prevalence of heart failure among individuals aged =65 is around 1%. CHF patients typically require multiple drugs for co-existing conditions. ADEs are implicated in about 6.5% of unplanned hospital admissions and occupy approximately 4% of hospital beds in the UK, with a significant share attributed to DDIs[8].

Treating cardiovascular conditions like hypertension, ischemic heart disease, and heart failure necessitates polypharmacy, which is now the standard treatment approach[9]. These patients are often older and face multiple conditions-such as diabetes, hypertension, COPD, and hyperlipidemia-which further increases medication use[9]. Hence, polypharmacy becomes inevitable for achieving therapeutic targets[9]. However, with an increase in medication numbers, the risk of adverse reactions grows exponentially due to DDIs[10]. Critically ill, chronically ill, and elderly individuals are particularly vulnerable to these interactions[10].

Cardiovascular drugs are frequently linked to PDDIs[11]. For instance, warfarin is known to cause fluctuations in prothrombin time[11], and serious consequences like reinfarction or bleeding can result from DDIs involving antiplatelet drugs such as aspirin and clopidogrel[11]. Advanced age is also a key risk

factor, as older individuals are more likely to have chronic conditions and be on multiple medications[11].

This pattern likely mirrors the situation in Nigerian CHF patients. Particularly concerning are DDIs that lead to severe hypotension or arrhythmias. Common signs of such interactions include nausea, headache, dizziness, and gastrointestinal upset.

Currently, no comprehensive studies have examined DDIs in Nigerian patients with CHF. This study aims to fill that gap by scientifically analyzing DDIs among heart failure patients in Nigeria.

MATERIALS AND METHODS

Study Area: The study was conducted at the Lagos University Teaching Hospital (LUTH), Idi-Araba-one of Nigeria's major Federal Government tertiary hospitals. LUTH serves as a referral hub for other health institutions within and beyond Lagos State and functions as a key training facility. It began with a 330-bed capacity and has expanded to accommodate 761 beds. Affiliated with the College of Medicine, University of Lagos, LUTH is responsible for the training of numerous medical, dental, pharmacy, and allied health professionals. The hospital also provides postgraduate training for doctors, nurses, and laboratory technologists.

Study Participants: The study involved adult male and female patients diagnosed with chronic heart failure (CHF) who attended the medical clinic at LUTH. CHF diagnoses were based on the International Classification of Diseases, 10th Revision (ICD-10), specifically codes I50.0–I50.9, I42.0–I42.9, and I11.0-I11.9. Inclusion criteria covered all chronic heart failure patients receiving care at LUTH who provided informed consent to participate. Exclusion criteria included patients with fewer than two medications prescribed during their clinic visit, admission, or discharge, and those with incomplete medical records related to prescribed medications.

Study Design: This investigation was designed as a hospital-based cross-sectional study aimed at assessing the prevalence and types of drug-drug interactions (DDIs) among chronic heart failure patients classified as ACC/AHA stages 3 and 4, who were receiving treatment at LUTH.

Sample Size Determination and Sampling: The sample size was calculated using the Cochrane formula, which is:

$$N = \frac{Z^2 PQ}{D^2} (12)$$

Where p is the prevalence of drug –drug interactions in and is 0.065 (Roblek *et al*., 2014)

Q = l-p

Q = O.94

Z is 95% confidence level which is 1.96

D is degree of accuracy required which is 5%

D = 0.05

$$N = \frac{1.96^2 \times 0.065 \times 0.94}{0.05 \times 0.05}$$

$$N = \frac{0.2347218}{0.0025}$$

N = 93.88

Adjusting for non-response rate of 20%

100%-20% =80%

=93.88/0.80

=117

The sample size was rounded off to 117

Data Collection Methods: Information was gathered using a structured, anonymous, interviewer-administered questionnaire. Data extracted from patient medical records included demographic characteristics (age, sex), clinical parameters (heart rate, blood pressure), coexisting medical conditions, laboratory values (such as serum creatinine and hemoglobin levels), the number of diagnoses per patient, and the duration of hospital stay. Medication data, including prescriptions at admission and discharge, were obtained from patient discharge summaries.

Data Analysis: To assess potential drug-drug interactions (DDIs), we used the Lexi-Interact database provided by Lexi Comp. This tool offers comprehensive details on the risks, pharmacokinetic and pharmacodynamic implications, and mechanisms underlying DDIs[7,13]. It also gives clinical recommendations for managing DDIs and references supporting literature[7,13]. Only clinically relevant interactions-categorized as types C, D, and X-

were included in the analysis, based on prior studies highlighting their significance[14,15]. We also examined combinations involving ACE inhibitors, ARBs, and aldosterone antagonists. Renal function was estimated using serum creatinine to stratify patients accordingly.

Statistical analysis was carried out using SPSS. Descriptive statistics were employed to summarize patient demographics. Means and standard deviations were calculated for continuous variables like age, hospital stay duration, number of diagnoses, and number of medications prescribed. Categorical variables (e.g., sex, number of medications at admission and discharge) were analyzed using frequency distributions. The proportion of patients prescribed cardiovascular drugs by pharmacologic class was also determined.

The average number of medications and potential clinically significant DDIs per patient was calculated. McNemar's test was applied to compare the number of patients with at least one clinically relevant DDI (type C, D, or X). Independent t-tests were used to compare the mean number of significant DDIs between patients with only chronic heart failure and those with additional comorbidities.

Linear regression assessed the relationship between the number of significant DDIs (types C, D, and X) and factors such as total diagnoses, number of medications, and hospital stay length. Variables that were statistically significant in the bivariate analysis were included in a multivariate logistic regression to identify determinants of potential DDIs. Odds ratios with 95% confidence intervals were reported. Statistical significance was set at $p < 0.05$.

Ethical Approval: Approval to conduct the study was obtained from the Health Research Ethics Committee of Lagos University Teaching Hospital (LUTH), Idi-Araba. Informed consent was secured from all participants before data collection. Participant confidentiality was strictly upheld—no unauthorized individuals had access to the questionnaire data, no identifiable information was collected, and the data was used solely for research purposes.

RESULTS AND DISCUSSIONS

Based on the socio-demographic characteristics presented in Table 1, a total of 110 adult participants were enrolled in the study, resulting in a response rate of 94%.

Of the participants, 109 patients (99.1%) were on more than one medication, and 51 individuals (46.4%) experienced adverse drug interactions. The average number of medications taken was 3.92 ± 1.60.

From the table above, those who take between 3 to 4 drugs were prone to type C interaction while those who take up to 5 drugs were prone to type D interaction

This hospital-based cross-sectional study was conducted to assess the prevalence and types of potential drug-drug interactions (pDDIs) among chronic heart failure (CHF) patients (ACC/AHA stages 3 and 4) at Lagos University Teaching Hospital (LUTH). The study found a high prevalence of pDDIs, with 71.8% of patients affected. This figure is consistent with findings from a similar study in Ibadan, Nigeria, which reported potentially harmful drug interactions in 65% of patients[16]. Our analysis revealed a significantly greater risk of drug interactions among patients prescribed six or more medications (Relative Risk: 7.8, 95% CI: 6.9-9.5; $p < 0.001$). This is comparable to an Indian study where 71.5% of prescriptions included at least one DDI[17].

However, our findings were higher than those reported in another Ibadan-based study, which identified potentially harmful interactions in only 25% of the cohort, primarily involving ACE inhibitors with NSAIDs (53.3%) and with amiloride/ hydrochlorothiazide (22.6%)[18]. That study also found only 1.5% of patients experienced documented adverse reactions to ACE inhibitors, and serum potassium, urea, and creatinine were monitored in just 37% of patients[18].

Compared to international data, our observed prevalence was also higher than in Nepal (21.3%), where 48 hazardous interactions were identified-most commonly involving atorvastatin, enalapril, digoxin, furosemide, clopidogrel, and warfarin. The majority of these were of moderate severity and pharmacokinetic in nature[5]. Likewise, our findings exceeded those from Brazil, where studies reported pDDI prevalence ranging from 25% to 47.4% across various clinical settings[19-21]. One Brazilian hospital study showed 37% of patients were exposed to at least one interaction, with the most common pair being digoxin and furosemide (11%)[21].

Compared to a British study that identified 111 potentially serious DDI pairs-19% involving first-line drug classes-our results remain significantly higher[22]. A U.S.-based study reported a far lower DDI prevalence of 0.63% (95% CI: 0.51–0.75) among outpatient visits involving two or more drugs[23].

In contrast, our prevalence was lower than findings from Pakistan, where 91.1% of patients had at least one pDDI, with 86.3% having major and 84.5% having moderate interactions (11). It was also lower than a study at Golnik University Clinic in Slovenia, where patients had an average of 6.5 ± 5.7 potential interactions on admission and 7.2 ± 5.6 at discharge[7]. In Mexico, 80% of patients had prescriptions with at least one pDDI, and 3.8% received contraindicated drug combinations[24].

Table 1: Socio-demographic Characteristics of the Respondents

Variables age (years)	Frequency (n=110)	Percentage (%)
40-50	19	17.3
51-60	17	15.5
61-70	58	52.7
71-80	15	13.6
81-90	1	.9
Mean age =62.14+10.243		
Gender		
Male	49	44.5
Female	61	55.5
Marital Status		
Single	3	2.7
Married	73	66.4
Divorced	4	3.6
Widowed	30	27.3
Religion		
Christianity	76	69.1
Islam	33	30.0
Others	1	.9
Ethnicity		
Igbo	39	35.5
Yoruba	59	53.6
Hausa	12	10.9
Are you employed		
Yes	59	53.6
No	51	46.4
Education		
No formal education	3	2.7
Primary	9	8.2
Secondary	76	69.1
Tertiary	22	20.0

Table 2: Total number of drugs patients are taking and prevalence of drug-drug interactions

Total number of drugs currently taking	Frequency (n=110)	Percentage (%)
1	1	0.9
2	17	15.5
3	19	17.3
4	21	19.1
5	21	19.1
6	2	1.8
7	6	5.5
Mean number of drugs = 3.92+1.601		
Experiencing unpleasant signs and symptoms after taking all medication		
yes	51	46.4
no	23	20.9

Table 3: Relationship between the number of drugs prescribed and type of Pddi

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
A	11	3.55	1.809	.545	2.33	4.76
B	10	5.30	2.003	.633	3.87	6.73
C	61	3.74	1.436	.184	3.37	4.11
D	3	5.00	.000	.000	5.00	5.00
Total	85	3.94	1.614	.175	3.59	4.29

P <0.016

Table 4: Types of potential drug-drug interactions based on the Lexi-interact database

Types of potential drug-drug interactions	Frequency	Percentage (%)
A	17	15.5
B	15	13.6
C	75	68.2
D	3	2.7
X	0	0.0
Total	110	100.0

In our study, type C interactions were most common (68.2%), followed by type A (15.5%), type B (13.6%), type D (2.7%), and no type X interactions. Patients on 3-4 medications were more prone to type C interactions, while those taking five or more were more susceptible to type D.

These findings align with research from Slovenia, where 373 clinically relevant type C interactions were identified, along with 98 type D interactions-most frequently between ß-blockers and a-antagonists (12.3%), calcium carbonate and bisphosphonates (7.1%), and ACE inhibitors with allopurinol (6%)[7]. Their study also reported 45 type X interactions at discharge, involving drugs like quetiapine, clozapine, and haloperidol[7].

In our study, the most common interacting drug pair was frusemide and digoxin (27%). This contrasts

with a study in Ibadan where the leading pair was ACE inhibitors with amiloride + hydrochlorothiazide (34.7%)[16], and with the Slovenia study where loop diuretics and ß2 agonists (6.6%) were most frequent [7].

The mean number of drugs in our cohort was 3.92 ± 1.60, lower than the Slovenian study which reported a median of 6 medications on admission and 7 at discharge[7]. Similarly, a recent study involving 400 CHF patients (median age 79, 55.5% male) reported a median of two major interactions on admission and three at discharge[25]. Other reports also identify combinations of potassium-sparing diuretics with ACE inhibitors/ARBs, and aspirin with non-selective ß-blockers and ß2 agonists as high-risk interactions during hospitalization[21,25,26].

CONCLUSION

This study highlights a high prevalence of potential drug-drug interactions among chronic heart failure patients. Clinicians should avoid prescribing combinations known to cause clinically significant interactions. The routine use of reliable drug interaction databases or software tools is recommended to screen for and prevent harmful DDIs.

Declarations:

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Ethics Approval and Consent to Participate: Ethical approval was obtained from the Research and Ethics Committee of Alex EkwuemeFederal University Teaching Hospital, Abakaliki, Ebonyi State. Written informed consent was obtained from all participants, and confidentiality was strictly maintained.

Competing Interests: The authors declare no conflicts of interest.

Consent for Publication: Not applicable.

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