# THE STUDY OF THE EFFECTS OF ANTIPLATELET DRUGS ON HYPERTENSIVE PATIENTS: PRESCRIPTION ANALYSIS STUDY

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**خلاصہ**

دیگر ادویات کے ساتھ antiplatelet دواءوں کا استعمال کرنے والے مریضوں میں تشخیص کی غلطیوں کو سمجھنا اور اس کے نتیجے میں فشار خون کے مریضوں میں ممکنہ ادویات کا دیگر ادویات کے ساتھ interaction کی تعداد کا اندازہ لگانا ہے- جیسا کے اودیات کا ادویات کے ساتھ مداخلت کا معاملہ بہت وسیع ہے اس کے ساتھ ادویات کے نسخوں میں غلطیاں نہ صرف پسماندہ بلکہ ترقی یافتہ ممالک میں بھی بیماری اور ہسپتال میں داخلہ کا باعث بن رہی ہیں-

اس مطالعہ کا مقصد نہ صرف ممکنہ نسخوں میں غلطیوں کو کم کرنے کے لیئے توجہ مرکوز کرنا ہے بلکہ اگر ان کو نظر انداز کیا جائے تو ممکنہ طور پر یہ drug-drug interaction کے غیر منفی اثرات اور مداخلت کا باعث بن سکتی ہیں

اس گزشتہ مطالعہ کو کراچی کے مختلف ہسپتالوں اور کلینک میں outpatient مریضوں پر کیا گیا ہے جن کے نسخوں میں فشار خون کی ادویات کے ساتھ اسپرین اور clopidogrel تجویز کی گئی ہے اس مطالعہ کے اعداد شمار کا تجزیہ PSS S سافٹ ویئر پر کیا گیا ہے NCCMERP (National Co-ordinating Council for Medication Error Reporting and Prevention) ادویات کی غلطیوں کی شدت کا اندازہ کے انڈیکس سے لگایا ہے-

موجودہ مطالعہ میں 1142 دواءوں کے غلط استعمال کا رجحان تین سو (300) نسخوں میں کیا گیا- جس سے اندازہ لگایا گیا کہ سب سے زیادہ غلطیاں مریض کے وزن کو دواء تجویز کرتے ہوئے نظر انداز کرنے کا تناسب 95.3 فیصد جبکہ دواء کا دواء کے ساتھ interaction، 95 فیصد ہے -مرض کی جانچ کی کمی 73.3 فیصد نسخوں میں دیکھی گئی-اوسطاً تجویز ہونے والی دواءئیوں کی سطح 5.64 ہے- جبکہ NCCMERP کے مطابق ٪ (64.33،3) =n 19 کیٹیگری D میں آتا ہے۔جو کہ مزید کیٹیگری C اور I کے زمرے میں آتا ہے۔ان تین سو نسخوں میں درمیانی درجے کے drug-drug interaction کی شرح 88.33 فیصد جبکہ معمولی نوعیت کے interaction کی شرح 56 فیصد اور سنگین نوعیت شرح 11 فیصد ہے.

موجودہ مطالعہ سے یہ بات اخذ کی جاتی ہے کہ ڈاکٹروں کے نسخوں کو تجویز کرنے کا عمل نہ صرف انتہائی ناقص ہے بلکہ غیر ضروری دواء استعمال کروانے کی وجہ سے دواء کا دواء سے interaction کے مواقع بڑھ جانے کا باعث بن رہے ہیں۔ جس سے مریضوں میں دواء کو صحیح انداز سے استعمال نہیں کیا جارہا-موجودہ تحقیق اس بات کا تجزیہ کرنے کے لئے خاص اہمیت کی حامل ہے کہ نسخوں کی غلطیوں اور غیر ضروری دواؤں کا استعمال کس طرح سے ہو رہا ہے۔

**Abstract**

The aim of the present study is to assess the prescribing errors inhypertensive outpatients taking Antiplatelet drugswith other drugs and consequently the frequency and pattern of potential drug-drug interactions. A retrospective study was conductedfrom December 2017- May 2018.The data analysis was carried out by SPSS. Potential drug-drug interactions were determined by Micromedex 2. Severity of errors was evaluated according to NCCMERP (National Coordinating Council for Medication Error Reporting and Prevention). In current study 1142 medication errors (MEs) were trailed in 300 prescriptions. The utmost ubiquitous ME was the patient's weight not mentioned in (95.3%) prescriptions continued by drug-drug interactions (95%). Diagnosis was missing in (73.3%) prescriptions. The average number of drugs per encounter was 5.64. According to NCCMERP highest number of the prescriptions (n=193, 64.33%) were fall in category D, followed by category C and I. Out of 300 prescriptions, majority of thedrug-druginteractions (88.33%) were moderate, (56%) minor andmajor drug-drug interactions were present in (11%) prescriptions. The most common drugs responsible for DDIs were Acetyl salicylic acid followed by Atenolol. The most commonly interacting pairs were Acetyl salicylic acid-Clopidogrel168(56%) followed by Acetyl salicylic acid-Captopril68(22.66%) and Acetyl salicylic acid-Nitroglycerine38(12.66).The study indicates the serious deficient of prescription writing skills among the doctors and their outcomes are responsible to promote the irrational use of drugs, high chances of drug-drug interactions and low patient compliance.

**Keywords:** Prescribing errors, Drug-drug interaction, Micromedex, NCCMERP, Hypertensive, Antiplatelet.

## Introduction

Medication errors are the most pervasive type of medical error, and cardiovascular drugs prescribed to hospitalized patients report for maximum number of these errors. A substantial body of evidence confirms the risk resulting from ME(Bates *et al*., 1995, Bates *et al*., 1993, Leape, 1995). Prescription is a written order by physician, consultant or dentist for the treatment of a disease. Prescription error is described as "negligence in the prescription writing practice that lead to adverse effects and potential drug-drug interactions". Prescribing errors includes selection of wrong drug, dose and route of administration (Bootman*et al*., 2006, Keers*et al*., 2013). Although the importance of good quality prescriptions has been approved worldwide but even the incidence of prescribing error is very high both in developed and underdeveloped countries (Blatt *et al*., 1997, Francois *et al*., 1997). According to researchphysicians, consultant, pharmaceutical companies and health professionals are relatively answerable for the irrational prescribing patterns (Fretheim, 2003).Due to frequent use of drugs possibility of human errors increase the frequency and risk of adverse events. DDIs may be responsible for severe adverse drug events and harmful results leading to patient morbidity and hospitalization. Different studies have reported that approximately 3% of hospital admissions are caused by DDIs (Jankel and Fitterman,1993, McDonnell and Jacobs, 2002, Peyriere*et al*., 2002). The most of the drug- drug interactions occur due to irrelevant consideration of prescriber or because of lack of knowledge of prescription writing practices(Askari et al., 2012, Ko et al 2008). Patients with hypertension are particularly vulnerable to DDIs due to their advanced age, gender, polypharmacy, increasing length of hospital stay, and the influence of heart disease on drug metabolism. The DDIs potential for a particular anti-hypertensive drug varies with the individual, the disease being treated, and the extent of exposure to other drugs. The present study was designed to assess the incidence and pattern of clinically significant DDIs in hospitalized hypertensive patients at a superspeciality hospital, with the assessment of reaction characteristics, outcome and management.

## Materials and Methods

The present retrospective study was conducted from December 2017 to May 2018 at superspeciality hospitals and clinics of Karachi, Pakistan after taking due permission from Ethical Review Board, Hamdard University, Karachi.

**Data Manipulation:** The stages of data manipulation were data collection, data analysis and evaluation of prescription errors.

Inclusion and Exclusion Study Criteria

Hypertensive patientsof either sex attending outpatient in hospitals and in clinics receiving Antiplatelet drugs with other drugs. Patients and their caregiver who were not interested to participate in the present study and those who visit in-patient unit were also excluded.

**Collection of Data:** All data were collected from superspeciality hospitalsand clinics. Out of 365collected prescription order 300 were selected. The prescriptions that were not clearly written and did not meet the inclusion criteria were excluded from the study. Demographic details, diagnosis, medication history and other information's were collected from patient's prescription and case record sheath.

**Data Analysis:** After collection of prescriptions they were analyzed and evaluated for the presence of essential elements of the prescription order (Lofholm and Katzung, 2001, BNF, 2000). A complete prescription encounter should contain patient's age, gender, weight and height. Non-proprietary and brand name of drug, medication strength, type of dosage form, amount to be dispensed in metric units, route of administration, duration of therapy, drug dosage, medication purposes and number of authorized refill if any (Smith and Enright, 2005).

**Evaluation of Prescriptions:** Prescriptions were evaluated for the presence or absence of medication errors. In current study prescription orders were also observed for drug-drug interactions by using Micromedex electronic database system. Micromedex contains a separate section on DDIs known as the Drug-REAX System. On entering the drugs one by one, the program lists the possible DDIs and categorizes DDIs according to their interaction effect, severity and grouped into minor, moderate and major drug-drug interactions (Micromedex, 2007).

According to NCCMERP Index medication errors were categorized (NCCMERP, 2001). NCC MERP index comprises nine discrete categories ranging from A (circumstances or events that have the capacity to cause error) to I (an error occurred that resulted in the patient's death). Binary logistic regression analysis and Odds ratio were performed to determine the incidence of drug-drug interactions and their correlation with polypharmacy.

**Results**

In present study 1142 medication errors were indentified in 300 prescriptions. In maximum number of prescriptions (95.3%, n=286) patient's weight was not cited, followed by drug-drug interactions (95%, n=284) and patient's diagnosis (73.3%, n=220) presented in Table 1. In all selected prescriptions average number of drugs per prescription was 5.64. In maximum number of prescriptions 3 drugs were prescribed. Five drugs were prescribed in (24.66%) prescriptions and then four and six drugs were in (23%) and (21.33%) prescriptions, respectively, Fig.1. Pearson correlation and Binary logistic regression were performed to determine the incidence of drug-drug interactions and their correlation with number of drugs. Significant correlation was observed ($\chi^2$=17.62, p=0.0001) for those prescription orders having more than 5 drugs, Fig.2. This reveals that the errors like drug-drug interactions were significantly grow with increase in number of drugs per prescription.

NCC MERP adopted a Medication Error Index that classifies an error according to the severity of the outcome. In accordance with the NCCMERP Index, out of the three hundred prescriptions, only (11.66%, n=35) prescriptions were placed in most severe category I. Maximum number of prescriptions (64.33%, n=193) were placed in category D, and in category B smallest number of prescriptions (1.6%, n=5) were found, Fig.3.

This study indicates that drug-drug interactions were significantly increased with prescriptions having more than 5 drugs. All drug-drug interactions were grouped according to Micromedex. Micromedex is an online evidence-based database that includes "in-line" referenced information about drugs, toxicology, diseases, acute care, and alternative medicine for healthcare professionals.

In current study according to Micromedex most of drug-drug interactions (88.33%, n=265) were moderate, some (11%, n=33) were major and (56%, n=168) were minor drug-drug interactions, Fig.4.

The most common drugs responsible for potential DDIs were Acetyl salicylic acid followed by Atenolol. The most commonly interacting drug pairs were Acetyl salicylic acid-Clopidogrel 168(56%) followed by Acetyl salicylic acid-Captopril 68(22.66%) and Acetyl salicylic acid-Nitroglycerine 38(12.66) presented in Table 2.This study indicates the serious deficient of prescription writing skills among the doctors and their outcomes are responsible to promote the irrational use of drugs, prescribing errors and high chances of drug-drug interactions (DDIs) due to polypharmacy and low patient compliance.

**Discussion**

Hypertension is the major chronic health issue in developed and underdeveloped countries leading to high mortality and morbidity rate worldwide (Collins et al., 1990, Hansson, 1996). It is a salient risk factor for cardiovascular diseases e.g. stroke, heart failure, angina, myocardial infarction (Neal *et al*., 2000).Medication errors are frequently found in the prescribing patterns of hypertensive patients and those results in high damage and sometimes death. At least 1.5 million people are victimized every year due to unprofessional behavior (Institute of Medicine, 2007). In Pakistani population cardiovascular diseases is one of the serious problem due to hypertension but a better management of the risk factors can reduce the mortality rate (http://www. Dailytimes.com.pk). In present study, out of three hundred prescriptions 62.73%, 95.3% and 49.3% prescriptions were not mention the patient's age, weight and gender, respectively. Similar results were reported from other studies (Nesar et al., 2014, Nesar *et al*., 2015). During the present study it was also noted that error of omission was found in 0.7% prescriptions. Other investigator also reported this type of omission of drug/dose and dosage form errors (Pote*et al*., 2007). In the present study wrong strength of drug was found in 2% prescriptions and diagnosis of patient was missing in 73.3% prescriptions contributing to the third most frequent ME. Previously other study also reported that 69.58% prescriptions were missing the patient's diagnosis (Ghoto*et al*., 2013). Average number of drugs per prescription was 5.64. Similar result was also reported from another study (Nesar et al., 2018). Five drugs were prescribed in (24.66%) prescriptions and then four and six drugs were in (23%) and (21.33%) prescriptions, respectively.

Pearson correlation and binary logistic regression was applied to analyze prescription for DDIs and found that prevalence of DDIs is remarkably amplified as there is an increase in number of drugs per prescription (($\chi^2$=17.62, p=0.0001*). This indicates that the errors like drug-drug interactions were significantly grow with increase in number of drugs per prescription. Prescriptions containing $\geq$ 5 drugs increase the odds ratio by 8.514. It means the prescriptions containing more than 5 drugs are 8.5 times more prone to DDI than the prescriptions containing less than 5 drugs.

The medication errors analyzed during the present study were also classified on the basis of NCCMERP category. Most of the prescriptions (n=193, 64.33%) were fall in category D, followed by category "C" in which (50, 16.66%) prescriptions were fall. Minimum number of prescriptions (n=35, 11.66%) were categorized in most severe class I.

For classification of drug-drug interaction all prescriptions were analyzed according to Micromedex.88.33% drug-drug interactions were moderate and 56% minor drug-drug interactions. Major drug-drug interactions were present in (11%, n=33) prescriptions. The observations of present study identified that

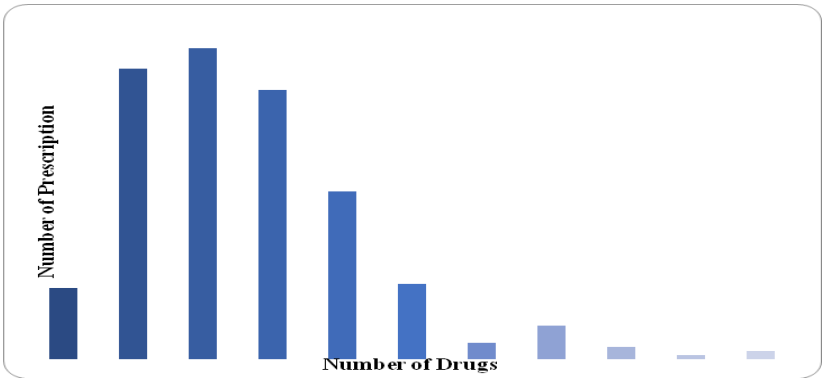


**Fig.1. Prescriptions having different drugs prescribed with Antiplatelet**

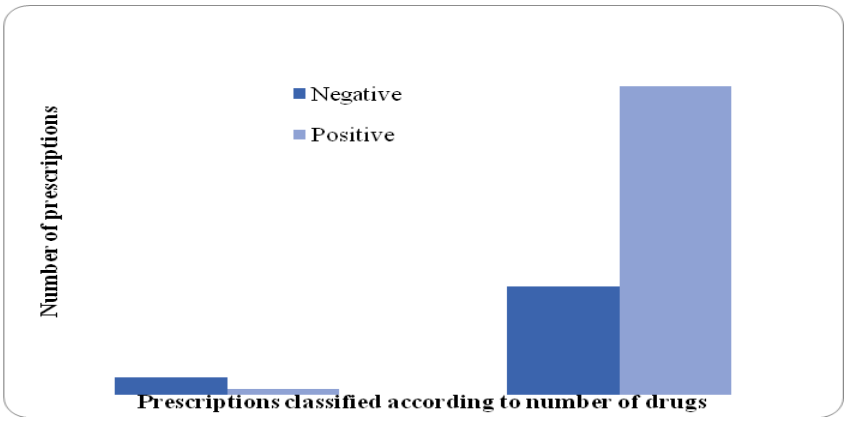


**Fig.2. Prescription classified according to number of drugs* drug interaction by SPSS**

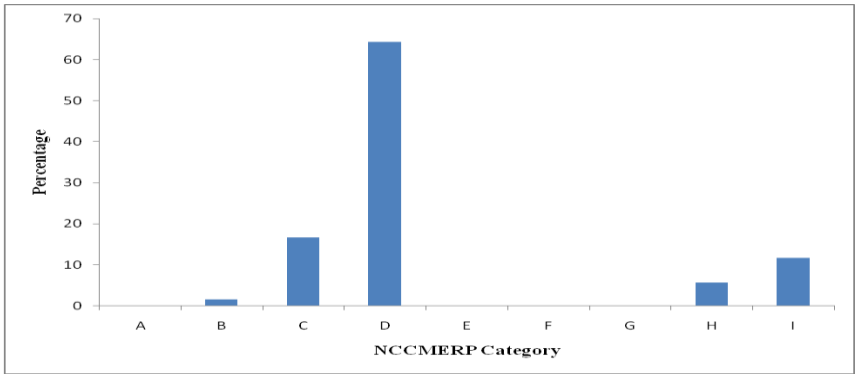


**Fig.3. Severity index of 300 prescriptions of Antiplatelet according to NCCMERP**

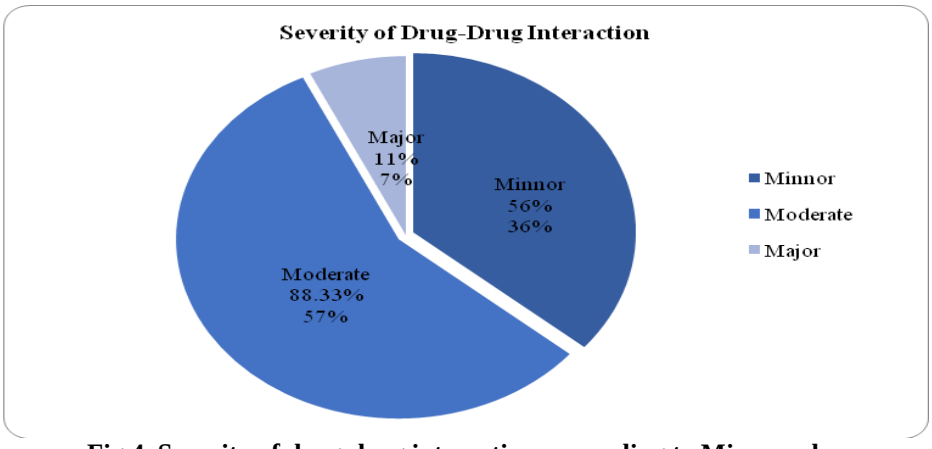


**Fig.4. Severity of drug-drug interactions according to Micromedex**

acetyl salicylic acid and Clopidogrel are the most commonly prescribed antiplatelet drugs among hypertensive patients. Similar study was carried out in 2011 related to the medication errors in hypertensive and diabetic patient prescriptions (Khalid*et al*., 2011). Other study also reported potential drug-drug interactions in 80.4% of the prescriptions (Nesar *et al*., 2015).The current study was planned to evaluate the medication errors and potential DDIs among medication prescribed to hypertensive patients.The studies like the present are extremely significant for analyzing the erroneous prescribing pattern and rational use of drugs.

**Table 1:Medication errors in Antiplatelet prescriptions**
**Number of prescriptions (n=300)**

| Name of Errors | Incidence of error N (%)[a] |
|---|---|
| Ambiguous medication order | 7(2.3) |
| Patient age not given | 188(62.73) |
| Patient weight not given | 286(95.3) |
| Patient sex not given | 148(49.3) |
| Mis-spelling of medicine | 1(0.33) |
| Error of Omission | 2(0.7) |
| Writing wrong strength or no strength of medicine | 6(2) |
| Drug-Drug interaction | 284(95) |
| Missing diagnosis | 220(73.3) |

[a] = Number and percentages of prescriptions having medication error.
Errors, which were 0%, are not mentioned.

**Table 2: Five most Common Drug combinations having Potential Drug-Drug Interactions**

| S.No | Drug combination | N (%) |
|---|---|---|
| 1 | Acetyl salicylic acid+ Clopidogrel | 168(56) |
| 2 | Acetyl salicylic acid + Nitroglycerine | 38(12.66) |
| 3 | Acetyl salicylic acid+ Captopril | 68(22.66) |
| 4 | Atenolol + Metformin | 8(2.66) |
| 5 | Acetyl salicylic acid+ Furosemide | 35(11.66) |

## Conclusion

The present study report some deficiencies in the quality of prescription writing skills and common prescribing errors in outpatient settings in Karachi, Pakistan. Prevalence of potential drug-drug interaction is high in hypertensivepatients due to polypharmacy. The results showed alarming situation that needs an urgent and firm health-care facility in order to develop system to make prescribers alert about interactions, clinically relevant. Furthermore the implementation of electronic prescribing should be made possible to avoid errors during medication cycle.

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