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RESEARCH ARTICLE
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THE PHARMACOLOGICAL MAZE: UNCOVERING DRUG INTERACTION PATTERNS IN HYPERTENSIVE AND DIABETIC REGIMENS

Asfia Arooje[1*], Zill-e-Huma[2*], Maimoona Mushtaq[3], Tassawer-e-Meran[4], Waqar Siddique[5], Hassan Umar[6], Aqna Malik[7], Muhammad Naeem[8], Zainab Saddiqua[9], Faiza Tabbasum[10], Amir Jalal[11]

[1*,7,9,10]Department of Pharmacy, The University of Chenab, Gujrat, Pakistan;
[2*]Rashid Latif Medical College, Punjab, Lahore, Pakistan
[3]Department of Pharmacy, International Institute of Science, Art and Technology (IISAT);
[4]Faculty of Pharmacy, Superior University, Lahore, Pakistan
[5,6]Riphah Institute of Pharmaceutical Sciences, Riphah International University Lahore Campus, 54000, Lahore, Pakistan
[8]Chief Drugs Controller Office, Punjab, Lahore, Pakistan
[11]Sahara Medical College Narowal, Pakistan.

***Corresponding author(s):** Asfia Arooje & Zill-e-Huma
*Email((s): asfia@pharm.uchenab.edu.pk & huma.cheema1@gmail.com

ABSTRACT

Introduction: This assessment studied potential drug interactions in polypharmacy among diabetic and hypertensive (HTN) patients. Chemically purified drugs have significantly improved healthcare, but genetic variations among patients pose challenges in drug metabolism and response. Polypharmacy, common in managing chronic conditions like hypertension and diabetes mellitus (DM), increases the risk of drug-drug interactions (DDIs), altering drug efficacy or safety and complicating clinical management. DDIs can be pharmacokinetic, affecting drug absorption, distribution, metabolism, or elimination, or pharmacodynamic, involving synergistic or antagonistic effects at drug target sites. Hypertension and diabetes frequently coexist, increasing treatment complexity and the risk of adverse events.

Material & Method: Managing these conditions often requires multiple medications, raising the likelihood of DDIs and severe adverse effects. A study analyzed 500 prescriptions from hospitals in Lahore, Gujranwala, and Gujarat using the Lexicomp application to investigate potential DDIs (pDDIs).

Result: The analysis found that 81.56% of prescriptions contained at least one interaction, with 59.68% involving both DM and HTN. The average number of drugs per prescription was 3.68, and the average number of interactions was 4.46. C-type interactions, requiring monitoring, were most common at 66.53%, and moderate severity interactions constituted 60.22%. Notably, 3.36% were contraindicated, posing a high risk of severe adverse effects.

Conclusion: The findings highlight the need for vigilant prescription management in DM and HTN patients. Healthcare providers must carefully consider drug combinations, and pharmacovigilance is essential. Personalized medicine, tailoring treatments to individual genetic profiles, can help mitigate

polypharmacy risks. Pharmacists play a key role by analyzing prescriptions, adjusting doses, and recommending alternatives when necessary to improve patient outcomes and reduce healthcare costs.

Keywords: Polypharmacy, Drug interactions, Hypertension (HTN), Diabetes mellitus (DM), Pharmacokinetic, Pharmacodynamic, Adverse effects, Pharmacotherapy, chemically purified drugs, Genetic variations, Drug efficacy, Drug safety, Patient outcomes, Lexicomp, Prescription management, Pharmacovigilance, Personalized medicine, Contraindicated interactions, Healthcare costs, Pharmacist review

1. Introduction

Chemically purified drugs revolutionized the health care because they can be used for treatment and prevention of diseases for long time and help to quickly get rid of illness as compared to old remedies. The correct use of drugs to prevent and treat illness or disease is pharmacotherapy (1). It is difficult to achieve this goal due to genetic variations among people which make each patient unique from others. Consideration should be given to the patient related parameters e: g age, gender, ethnicity, economic status, religious beliefs etc. along with drug related parameters. For many individuals' multiple drugs usage (Polypharmacy) is essential and a rational therapy with undisputable benefits. However, no drug is completely free from harmful effect that is why the chances of reactions related to drug use and adverse drug reactions (ADR's) and ADRs as consequence of drug interactions also increases (2). Drug interaction is change in the pharmacological effect of a drug due to co-administration of another drug, food, supplement, beverage etc. It results in an amplified, weakened or completely changed effect of a drug. Drug-drug interaction is most common preventable error.

The concept of drug interaction evolved in 1960's. it was discovered that drug can interact with other substances which are co-administered with it. In 1970's pharmaceutical companies submitted annual reports related to drug interactions in the Swedish catalogue of approved medical products (FASS) (3). In 1997 a system classifying drug interactions was introduced in FASS and the system was according to clinical relevance and level of documentation. Today both the American Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have clear guidelines about the studies on drug interactions before its market approval.

1.1. Hypertension (HTN)

Hypertension, commonly known as high blood pressure, is a chronic medical condition characterized by persistently elevated blood pressure in the arteries. It is often termed a "silent killer" because it typically has no symptoms but can lead to serious health complications if left untreated (4). Hypertension is one of the most common cardiovascular conditions worldwide, affecting millions of people across all age groups.

1.1.1. Complications

Arterial Hypertension is a leading stimulus of CKD (5), atrial fibrillation (6), stroke, kidney failure, and heart failure (7) that vary from person to person.

1.1.2. Polypharmacy in HTN

HTN is treated by different classes of drugs. The drugs can be used alone or in combination with other medicines due to inadequate treatment and coexisting conditions like diabetes, stroke, kidney failure, and heart failure (8).

1.2. Diabetes Mellitus

Diabetes mellitus is a group of metabolic disorders characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. There are primarily two types of diabetes: Type 1 Diabetes: An autoimmune condition where the body's immune system attacks and destroys insulin-producing beta cells in the pancreas, leading to an absolute deficiency of insulin. Type 2 Diabetes: A more common form associated with insulin resistance and relative insulin deficiency. It

is strongly linked to obesity, physical inactivity, and genetic predisposition (9). Diabetes is a major public health issue, with Type 2 diabetes being the predominant form. It affects millions globally and is rising rapidly due to increasing rates of obesity and sedentary lifestyles (10).

1.2.1. Complications

Chronic hyperglycemia can lead to microvascular complications (such as retinopathy, nephropathy, and neuropathy) and macrovascular complications (such as cardiovascular disease and stroke) (11).

1.3. Interrelationship between Hypertension and Diabetes: Hypertension and diabetes frequently coexist, and their combination significantly increases the risk of cardiovascular events. For example, a high blood glucose level activates RAAS and increases angiotensin II levels. Increased angiotensin II levels cause vasoconstriction by retaining sodium and water in the blood vessels. This constriction causes vessels narrowing and ultimately high blood pressure (12). Patients with both conditions often require complex medication regimens, making them more susceptible to drug-drug interactions (DDIs). Effective management of these coexisting conditions is crucial to prevent complications and improve patient outcomes (13).

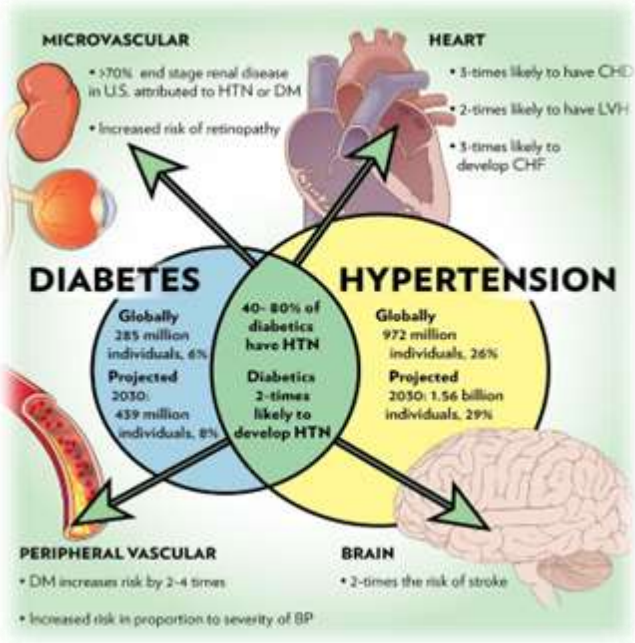

Figure 1. Comparison of Diabetes and Hypertension

According to Lago et al. (2007), individuals with diabetes are twice as likely to experience hypertension compared to those without diabetes (14). Hypertension associated with diabetes may develop due to oxidative stress, inflammation, endothelial dysfunction, and the activation of advanced glycation end products (AGEs) (15).Managing these two conditions simultaneously often involves multiple pharmacological treatments, known as polytherapy. Long-term polytherapy can lead to numerous drug–drug interactions (DDIs) (16). DDIs are major contributors to severe drug side effects and can result in significant morbidity or mortality, extended hospital stays, and increased healthcare costs if not addressed (17, 18).

1.4. Drug–drug interactions

Drug–drug interactions (DDIs) are the matter of great concern among the patients acquiring multidrug therapy. The World Health Organization accentuates that adverse drug reactions and their influence can be significantly reduced by inaugurating careful attention to the population at risk of DDIs (19). DDIs (drug-drug interactions) are classified into two types: pharmacokinetic and pharmacodynamic.

Table 1. Classification of drug interactions

Pharmacokinetic	Absorption
	Distribution
	Metabolism
	Elimination
	Drug transport
Pharmacodynamic	Synergism
	Antagonism

Pharmacokinetic drug interactions involve changes in drug absorption, distribution, metabolism, and elimination (20). To measure such interactions, parameters like serum concentration, drug half-life, and free/bound drug amounts must be considered.

1.5. Pharmacokinetics Drug Interactions

Absorption, primarily via the oral route, can be affected by factors such as gastrointestinal (GIT) motility, pH, drug PKa, physical state, surface area, and blood flow (21, 22). For instance, reduced antibiotic absorption leads to uneven drug levels, hindering infection treatment. Changes in drug absorption due to gastrointestinal motility, pH alterations, or microbial flora disruptions can impact drug effectiveness. Gastrointestinal motility alterations affect absorption rates, changes in pH influence drug availability (23). Weak acids/bases are absorbed differently based on pH changes (24). Antibiotics altering gut flora affect drug absorption and may impact vitamin K synthesis, altering drug effects like warfarin's anticoagulant action (25, 26).

Adsorption and chelation, crucial in drug interactions, involve formation of insoluble complexes. For instance, ciprofloxacin forms chelate with divalent/trivalent cations, reducing drug absorption (27). Antacids and charcoal bind drugs, delaying absorption. Concurrent administration of anticonvulsants with antacids decreases anticonvulsant absorption (28). In summary, pharmacokinetic drug interactions impact drug absorption, influenced by factors like GIT motility, pH changes, microbial flora disruptions, and adsorption/chelation processes, altering drug efficacy and patient outcomes (29).

Drug transport relies on membrane transporters like P-glycoprotein (P-gp) and CYP3A4 enzyme system (30). P-gp, found in enterocytes and hepatocytes, expels drugs, affecting their absorption and reducing plasma concentrations. Rifampicin induces P-gp, decreasing digoxin levels, while verapamil inhibits P-gp, increasing digoxin levels. P-gp in the blood-brain barrier influences drug distribution into the brain (31). Distribution interactions alter drug distribution patterns, often through protein binding alterations. Drugs can displace each other from protein binding sites, increasing free drug concentration and pharmacological effects. Examples include warfarin with phenylbutazone, leading to increased prothrombin time, and phenytoin with valproic acid, increasing phenytoin plasma levels and toxicity. Some interactions, like sodium bicarbonate with antidepressants, mitigate adverse effects by altering drug distribution (32). Metabolism interactions involve changes in drug metabolism, affecting drug duration and action. Cytochrome P-450 enzymes catalyze drug metabolism. Inhibitors like macrolides and inducers like rifampicin alter enzyme activity, affecting drug levels. For instance, phenytoin induces CYP3A4, decreasing quinidine concentration, while dexamethasone induces CYP3A4, diminishing artemether's antimalarial activity (33). These interactions impact drug efficacy and toxicity, highlighting the importance of understanding pharmacokinetics in clinical practice (31).

Table 2. Examples of cytochrome P450 enzyme system substrates

SUBSTRATE					
CYP1A2	**CYP2C19**	**CYP2C9**	**CYP2D6**	**CYP2E1**	**CYP3A4**
Amitriptyline	Clomipramine	Celecoxib	Amitriptyline	Acetamin-	Alprazolam
Caffeine	Cyclophospha mide	Diclofenac	Amphetamine	ophen Ethanol	Aripiprazole
Clomipramine	Diazepam	Flurbiprofen	Aripiprazole	Enflurane	Amitriptyline
Clozapine	Imipramine	Glipizide	Clomipramine	Halothane	Ca-channel
Cyclobenzaprine	Lansoprazole	Ibuprofen	Clozapine	Isofluran	blockers
Desipramine	Omeprazole	Irbesartan	Codeine		Carbamazepine
Diazepam	Phenytoin	Losartan	Tramadol		Dexamethasone
Haloperidol	Progesterone	Naproxen	Fluoxetine		Erythromycin
Imipramine	Propranolol	Phenytoin	Haloperidol		Imipramine
Olanzapine	Topiramate	Piroxicam	Hydrocodone		Ketoconazole
Propranolol		Rofecoxib	Imipramine		Midazolam
R-warfarin		S-warfarin	Metoprolol		Prednisone
Theophylline		Tamoxifen	Nortriptyline		Quinidine
Zileuton		Torsemide	Propranolol		Risperidone
		Valdecoxib	Risperidone		Tacrolimus
			Tamoxifen		Zolpidem
			Timolol		

Table 3. CYP 450 Inhibitors

INHIBITORS					
CYP1A2	**CYP2C19**	**CYP2C9**	**CYP2D6**	**CYP2E1**	**CYP3A4**
Cimetidine	Cimetidine	Amiodarone	Amitriptyline	Disulfiram	Amiodarone
Ciprofloxacin	Fluoxetine	Chloramphenicol	Cimetidine	Isoniazid	Azole
Clarithromycin	Lansoprazole	Cimetidine	Clomipramine		antifungals
Enoxacin	Omeprazole	Divalproex	Fluoxetine		Cimetidine
Erythromycin	Ritonavir	Fluconazole	Haloperidol		Ciprofloxacin
Grapefruit	Sertraline	Fluoxetine	Nefazodone		Diltiazem
juice	Topiramate	Itraconazole	Paroxetine		Fluoxetine
Isoniazid		Ketoconazole	Quinidine		Grapefruit
Ketoconazole		Omeprazole	Ritonavir		juice
Levofloxacin		Ritonavir	Sertraline		HIV protease
Norfloxacin		Sertraline	Venlafaxine		inhibitors
Ofloxacin					Macrolide
Paroxetine					antibiotics
					(except
					azithromycin)
					Norfloxacin

Table 4. CYP 450 inducers

INDUCERS					
CYP1A2	**CYP2C19**	**CYP2C19**	**CYP2D6**	**CYP2E1**	**CYP3A4**
Carbamazepie	Carbamazepine	Phenobarbital	Carbamazepine	Isoniazid	Barbiturates
Insulin	Phenytoin	Phenytoin	Dexamethasone	Retinoids	Carbamazepine
Omeprazole	Rifampin	Rifampin	Phenobarbital	Tobacco	Dexamethasone
Phenobarbital			Phenytoin		Ethosuximide
Phenytoin			Rifampin		Phenobarbital
Rifampin			Ritonavir		Phenytoin
Ritonavir					Prednisone
Tobacco					Rifabutin
					Rifampin

The kidney plays a crucial role in drug elimination, with drug-drug interactions often occurring during this process. These interactions can involve competition for transport sites, changes in glomerular filtration and renal blood flow, and alterations in urinary pH, impacting the excretion and efficacy of various drugs (34).

1.6. Pharmacodynamics Drug Interactions

Pharmacodynamic interactions are those in which the clinical effect of one drug is affected by the co-administration of another drug. The drugs influence each other's effects directly. The effect of a drug can be increased or decreased from its normal therapeutic level, called synergistic or antagonistic effect. The resulting interaction may occur at the receptor site and may be at a cellular, physiological or physiochemical level (35, 36). These are some mechanisms involved in Pharmacodynamics drug-drug interactions.

1.6.1. Synergism

A synergistic or additive effect is observed when drugs with similar pharmacological action or active ingredients are simultaneously administered. The receptor sites for the drugs involving in interaction may or may not be same. An example includes the increased risk of bleeding by the concomitant administration of clopidogrel with aspirin or other NSAIDs (37). Co-administration of theophylline and beta agonists such as albuterol increases the risk of cardiac arrhythmias (38). When amphotericin B is administered concomitantly with digoxin, hypokalemia and digoxin toxicity may occur (39). Some synergistic interactions are clinically beneficial, for example insulin is combined with oral hypoglycemic agents for achieving better control on blood glucose level, and combination of certain antibiotics are used to fight against complex infections (40, 41).

1.6.2. Antagonism

An antagonistic effect is observed when drugs with opposite pharmacological effect are administered simultaneously. These can also be beneficial in certain cases like benzodiazepine overdose or toxicity is cured by the antagonistic action of flumazenil and naloxone is used for opioid toxicity (42, 43). Antagonistic drug interactions can also be harmful, for example hypotensive action of beta blockers, diuretics and ACE inhibitors is inhibited by cyclo-oxygenase 2 (COX-2) inhibitors. Another example of antagonist drug-drug interaction is the co-administration of beta-agonists like albuterol and non-selective beta blockers like Propranolol (44).

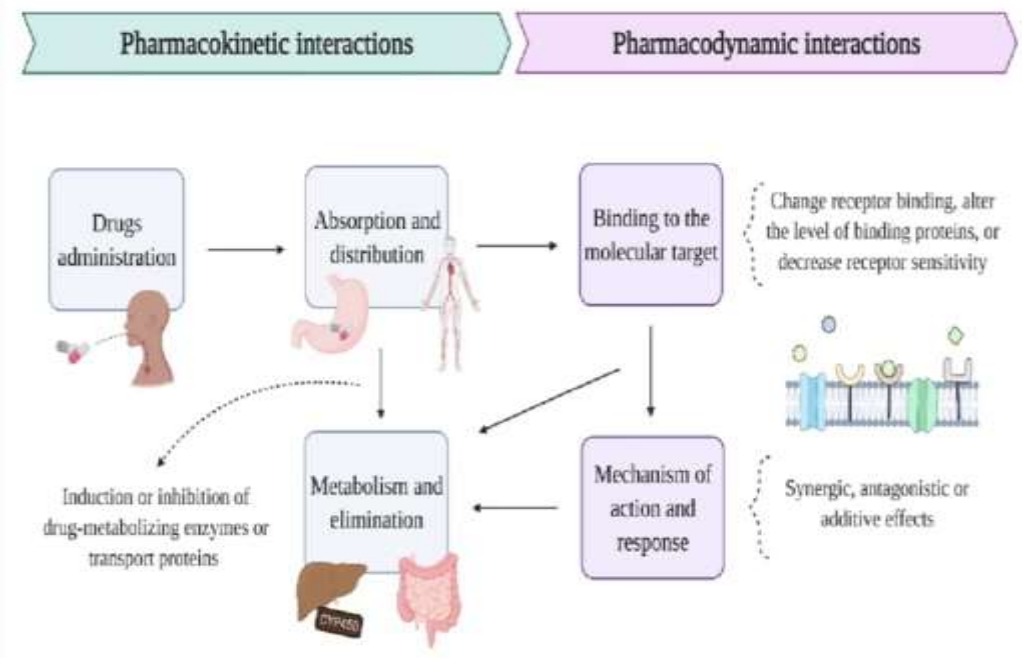

Figure 2. Pharmacokinetics and Pharmacodynamics

1.7. Epidemiology (45)

Particularly due to the change in the health care provision system prevalence of potential drug-drug interactions has been studied throughout the world with varied reports (46). Developed countries have reports of lesser prevalence of potential drug-drug interactions because of well-established health care provision and monitoring systems as compared to the developing countries where the health care provision and monitoring system is not well established. The application of epidemiology is the prevention of disease and promotion of health (47).

1.8. Prevalence of Potential drug-drug interactions at hospitals

Numerous studies have been conducted throughout the world in different hospitals at different levels in different settings to estimate the prevalence of potential drug-drug interactions in both in and out-patients. Different countries applied various techniques at different levels and presented their results after studies. Sweden has reported a study having 31% drug interactions in out-patients. Out of this 31% only 3% interactions were of major clinical significance and 23% interactions were of moderate importance (47).

America found 88% of prescriptions that contain more than 5 drugs have potential drug-drug interactions (48). In Mexico a study on elderly patient's prescription was conducted and it declared 80% potential interactions (48). Thailand conducted study for interactions in two departments. In psychiatric department prevalence was 57.8% while in outpatient setting it was 27.9% (49). In medical center of Taiwan, it was found to be 25.6% (50). Emergency department of a hospital in Canada reported 31% potential dug-drug interactions (51). American emergency department studies declared 47% interactions (52). It was found that as the number of drugs prescribed in a prescription increases the risk for interactions automatically increases. Prescriptions having 2 drugs have 13% prevalence but in prescription having more than 2 drugs prevalence was increased up to 80%. Italy reported that 11% patients must have a potential drug interaction (53).

In Dutch university prescriptions were analyzed and it showed 27.8 % patients have at least one potential drug-drug interaction (54). Moreover, it was found that nephrology department has more interactions than pediatric surgery. In UK potential drug-drug interactions were reported in 90% of patients but only 62% interactions were of major severity (55). Brazilian study suggested more interactions in cardiology and ophthalmology (56). Study report of Nepal shown 21.3% potential drug interactions (57). Study report of Iran has shown20.3% interactions (58). In Pakistan two studies were conducted in pediatric population to estimate potential drug-drug interactions and it reported 66.9% and 25.8% prevalence (59).

Table 5: Classification of DDIs based on severity and documentation

Level	Sub-classification	Outcome
Severity	Contraindicated	Simultaneous use of drug combination is contraindicated.
	Major	Due to life threating effect of this drug combination, requires intervention to prevent serious effects
	Moderate	Change in therapy is require because drug combination may worsen the patient condition
	Minor	Severity or frequency of an adverse effect may increase with drug combination but has no effect on the therapeutic effect of the drugs
Documentation	Excellent	Documentation of the DI is reported in controlled studies
	Good	Documentation is not reported in well controlled studies, but the interaction is strongly suggested in some studies
	Fair	Documentation is poor but interaction can be suspected on the basis of

2. Literature Reports

DDIs are major events that are important in both quality of patient life and quality of treatment strategy. In Iran not any specific method has been developed yet to analyze and prevent interactions. Focus of this study was re-analyzed occurrence & pattern & Prevention DDIs in Iran. For this purpose, multiple web sources including PubMed, Scopus, and electronic Persian databases, and Google Scholar were approached to find out Studies to point out published studies in Iran. In this method only published articles were again analyzed and reviewed. Inclusion criteria constitute only those studies which were based on original incidence of DDIs in inpatient or outpatient settings in Iran. Exclusion criteria was drugs and DDIs with herbs, diseases and nutrients' population of 1053 potentially eligible cites were selected. After applying exclusion criteria only 34 articles were found to be eligible.it is concluded that all studies just focused on PDDIs while no one on actual DDIs. The median incidence of potential DDIs in outpatient settings was 8.5% per prescription while it was 19.2% in inpatient settings. A critical feature was patient age. Common interacting class of drugs includes B-blocker, ACEIs and NSAIDs .out of selected 34 articles 31 includes observational studies while 3 were experimental. Almost every study have concluded that pDDIS are relatively high in Iran and more extensive research is necessary to further incidence of DDIs and to analyze these after effects preventive interventions should be recommended and used via usage of IT (60).

3. Materials & Method

In this discretional cross-sectional study prescriptions of patients were collected from LGH, PIC Lahore, Medcare international hospital Gujranwala and Ittefaq hospital Gujarat.

3.1. Sample

Total number of prescriptions that was collected and analyzed were 500 in number

3.2 Inclusion criteria

Prescription in which more than 2 medicines were prescribed, Prescriptions of male and female more than 30 years of age were selected, Prescriptions of patients suffering with DM, HTN, Both, DM with concomitant disease, HTN with concomitant disease were selected.

3.3. Exclusion Criteria

Prescriptions in which less than 2 medicines were prescribed, Prescriptions of male and female less than 30 years of age were selected, Prescriptions of patients suffering with other than DM, HTN, Both, DM with concomitant disease, HTN with concomitant disease were selected

3.4. Data Analysis

pDDIs were assessed by using mobile application Lexicomp and classified based on interactions, Risk rating, severity and reliability rating. It is considered one of the best performing DDIs screening program, several studies have assessed the performance of Lexicomp interact as a DDIs screening. Lexicomp interact was reported highly specific (80-90%) and sensitive (87-100%) among most of screening programs.

4. Result

A sample of 500 prescriptions was selected to evaluate pDDIs presents in these prescriptions. After analysis it is concluded that 81.5635% prescriptions contain pDDIs. Out of which were 59.68% DM & HTN prescriptions, 21.323% only HTN & HTN with concomitant diseases & 19.259% DM & DM with concomitant diseases prescriptions contains pDDIs. Average no of medicines per prescriptions were 3.682, avg. no of interactions per prescription were 4.46, avg. no of X-type interactions per prescription were 4.912 & %age of no. of interactions per prescription were 22.44%.On the basis of type of interaction, ratio of %age interaction of D-type is 22.9845,C-type 66.532%,B-type 9.543%, & X-type were 0.94%.On the basis of severity, ratio of %age interaction of Moderate type 60.215%,major type 26.52%, Minor type 9.901% and contraindicated type is 3.36%.similarly, on the

basis of Reliability, ratio of %age interaction of Excellent type 10.25%,Fair type 71.744%,good type 17.069% and poor type are only 0.94%.

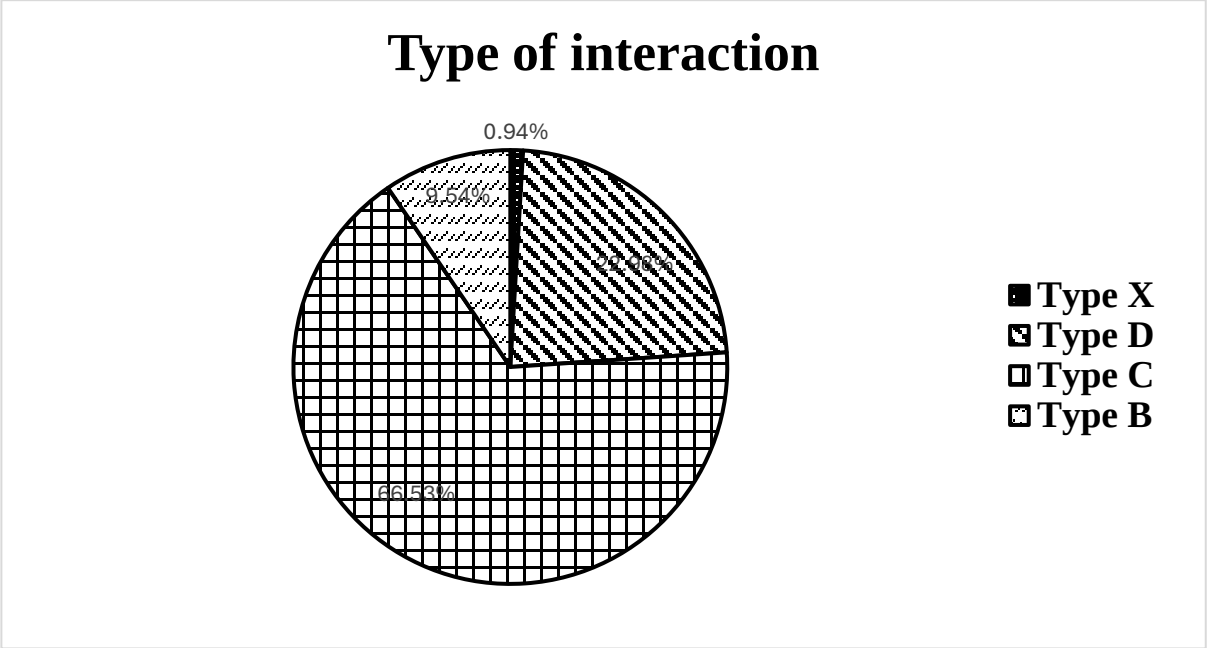

Figure 3. Type of interaction

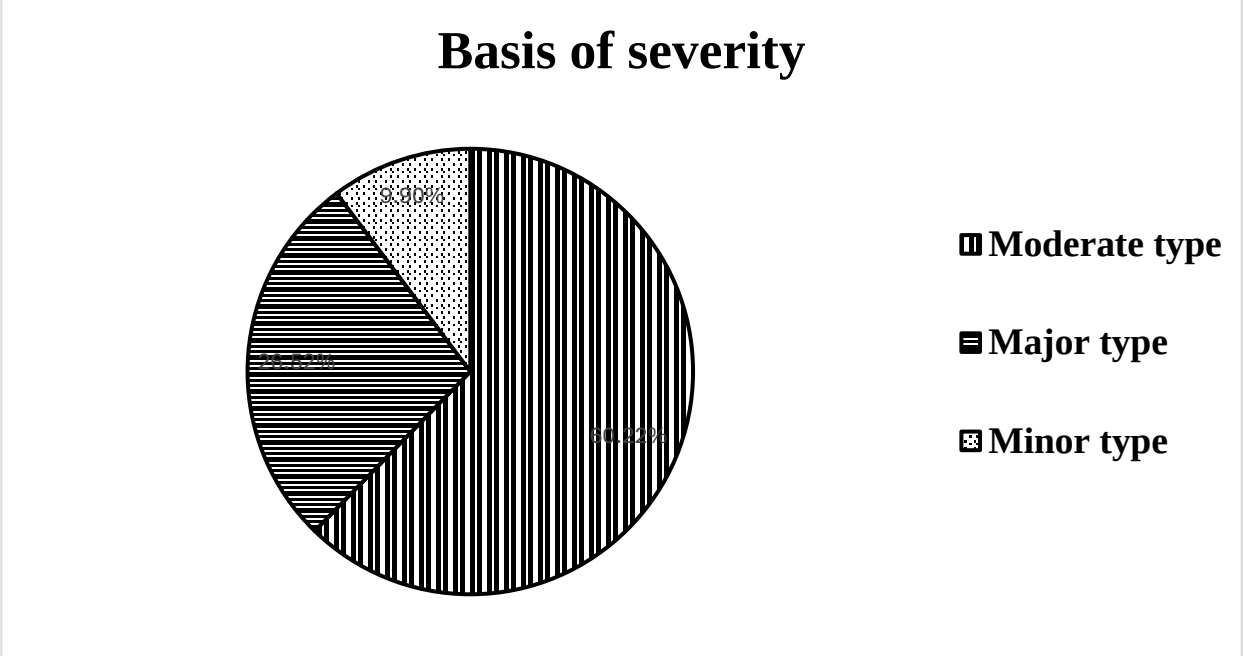

Figure 4. Basis of severity

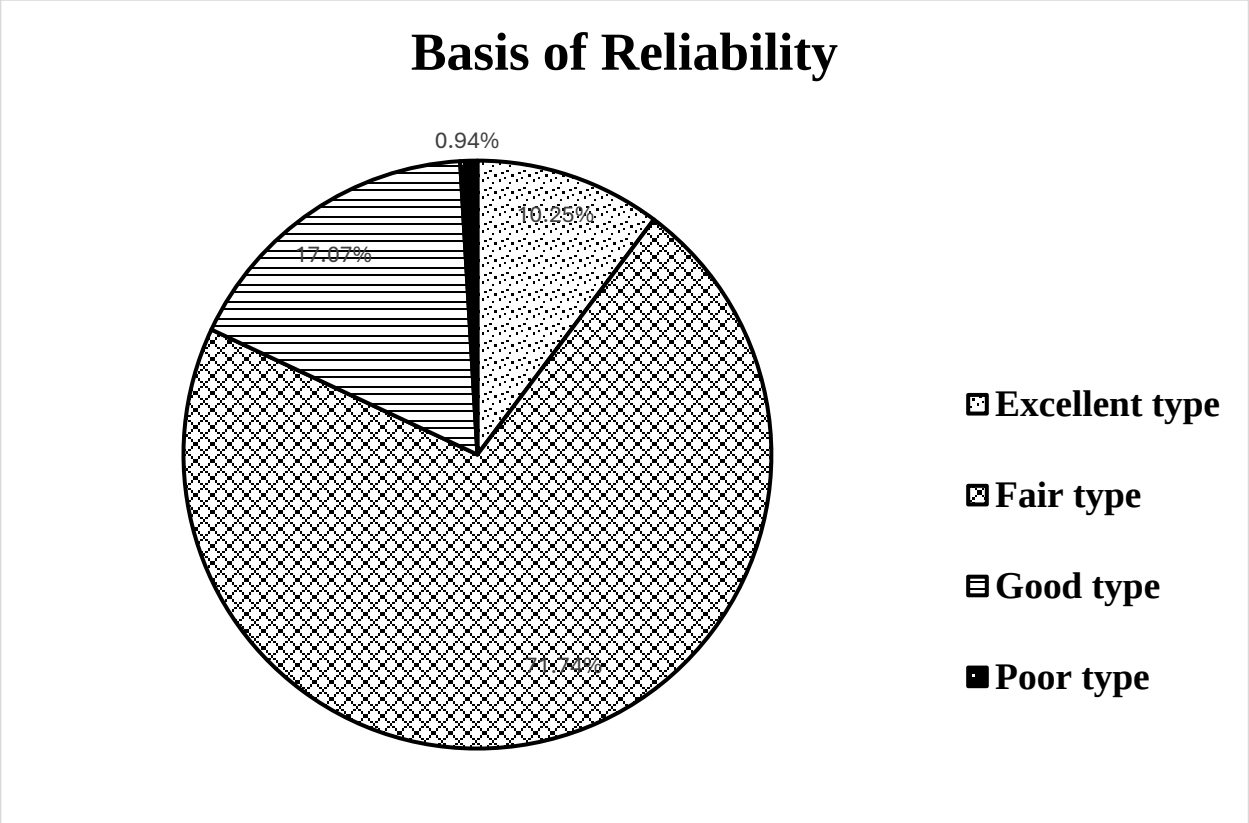

Figure 5. Basis of Reliability

5. Conclusion

A sample of 500 prescriptions was selected. After analyzing these prescriptions while keeping in mind inclusion criteria of clinical study it was founded that prevalence of Diabetes in patient with polypharmacy was 20.359%, Hypertension 25.748% while 53.892% patients were those who were diagnosed with both diseases (DM and HTN) and were having 2-12 drugs approximately.

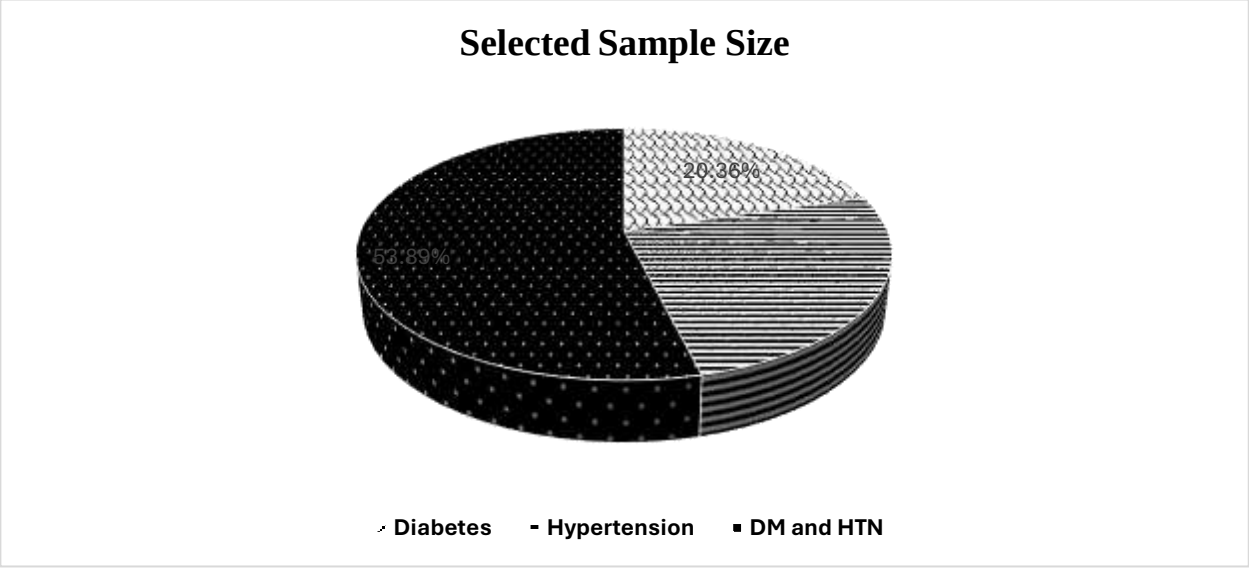

Figure 6a.Sample Size

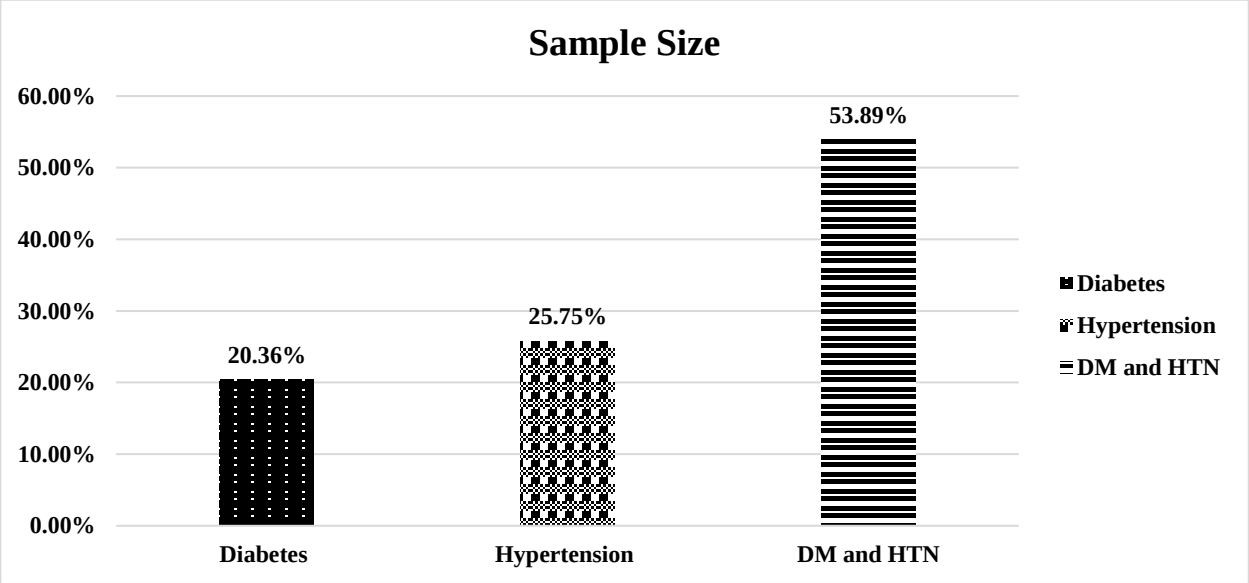

Figure 6b. Sample Size

After carefully analyzing all the prescription via Lexicomp by using interaction update column it is concluded that quality prescribing in that prescriptions was approximately 18.563% which means these prescriptions does not contain any type of drug interaction out of which 5.389% was those prescription which include diagnosis of both diseases DM and HTN while 8.383% was only of HTN and 4.79% was of DM. Similarly, Appearance of interactions in selected prescriptions was 81.437% out of which 59.568% was those which were of DM & HTN while 21.323% contains HTN and Concomitant diseases while 19.259% contains diagnosis of DM and Concomitant diseases. Total found no of interactions were 2232 in 500 prescriptions having no of medicines 1541.It is concluded that average no. of medicines per prescriptions are 3.082 and no of interactions per prescription is 4.46 while %age of no. of interactions per prescription is 22.44%. It is evident that X type Interactions per prescription is 4.912%. As Lexicomp also characterizes these interactions based on its type, severity, onset and reliability.

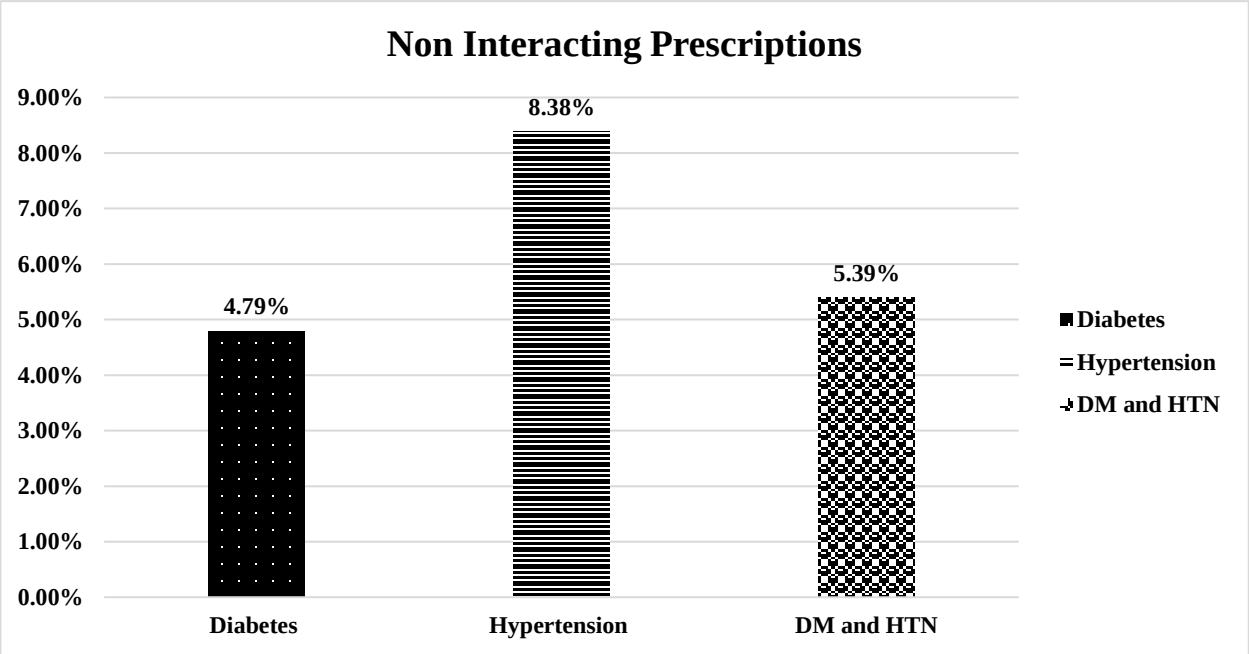

Figure 7. Non-Interacting Prescriptions

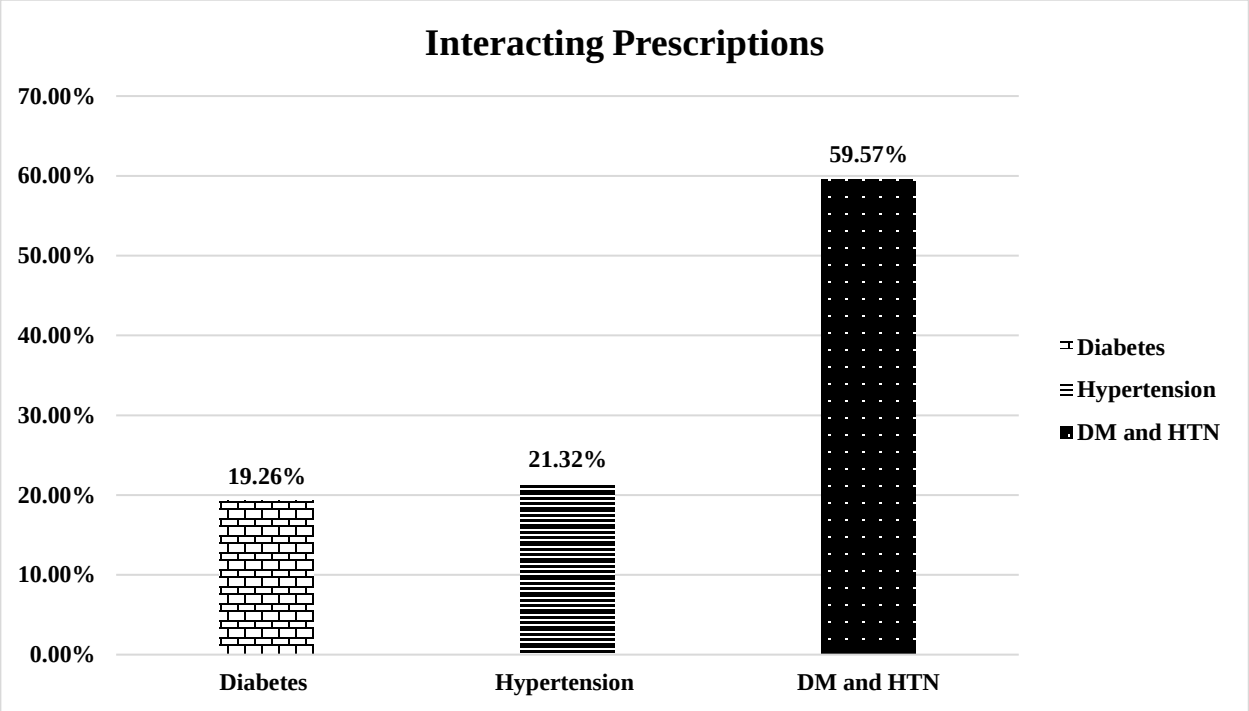

Figure 8. Interacting Prescriptions

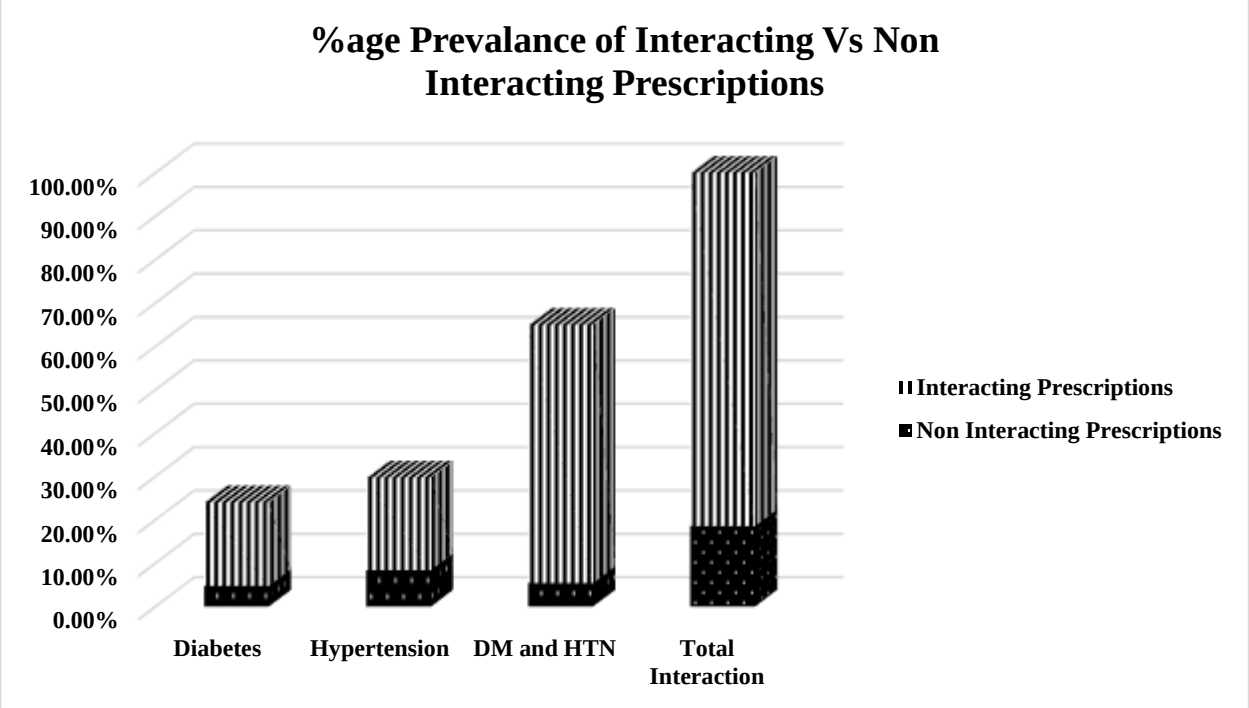

Figure 9. %age Prevalence of Interacting Vs Non-Interacting Prescriptions

Based on its type D-type interactions were 22.984%, C-Type Interactions were 66.532%, Btype Interactions were 9.543% and X-type interactions were 0.94%. Analysis based on Severity Drug interaction is classified into 4 classes respectively contraindicated, Major, moderate and minor. It is concluded that maximum no of interactions was of moderate level that's required constant and proper monitoring of patients for appearance of ADRs and ADE and in case of appearance of these interactions required therapy modification. %age prevalence of moderate type of drug interaction is 60.215%, major was 26.52% and minor was 9.901%. A shocking prevalence was appearance of contraindicated interactions that was 3.36%. The third type of classification is on the basis of reliability according to which DDIs are classified into 4 categories that are Excellent, Good, Fair and

poor. On this base %age prevalence of Excellent drug interaction are Excellent ratio is 10.25% while more prevailed DDIs are of fair type with % age prevalence 71.744% appearing as more common and Dangerous one. While remaining two are good type (17.069%) and Poor are 0.94% which can be ignored.

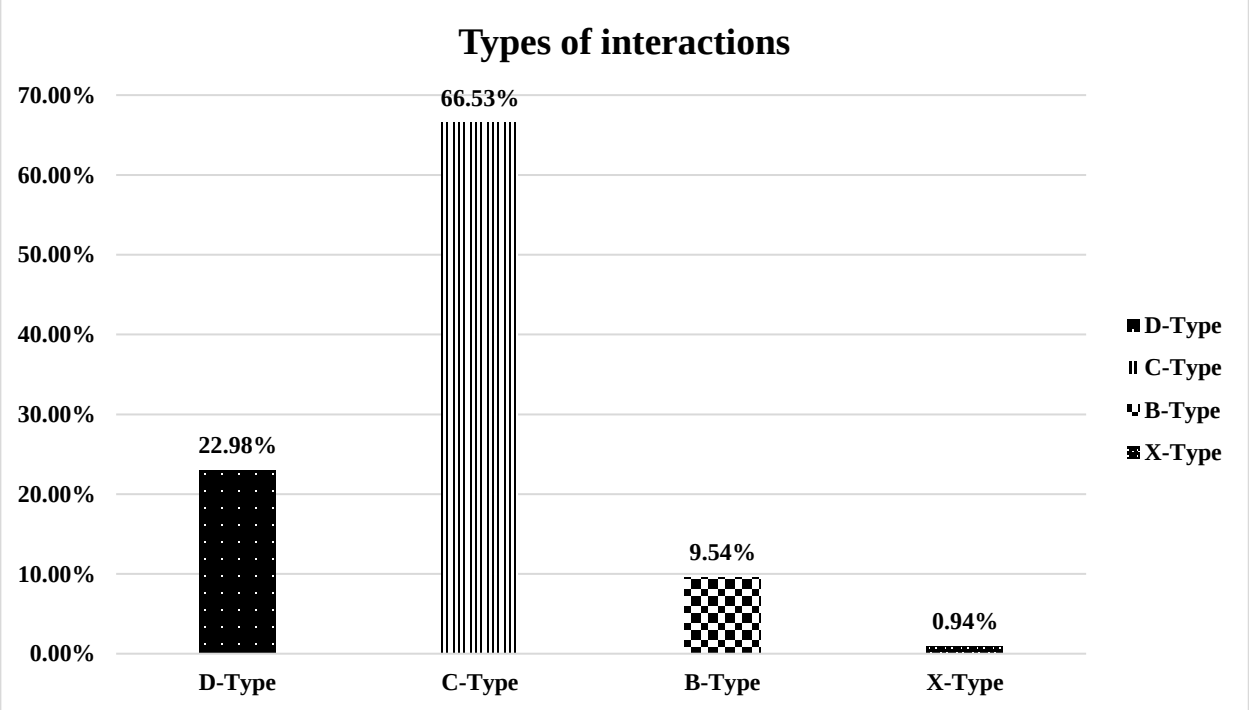

Figure 10. Types of interactions

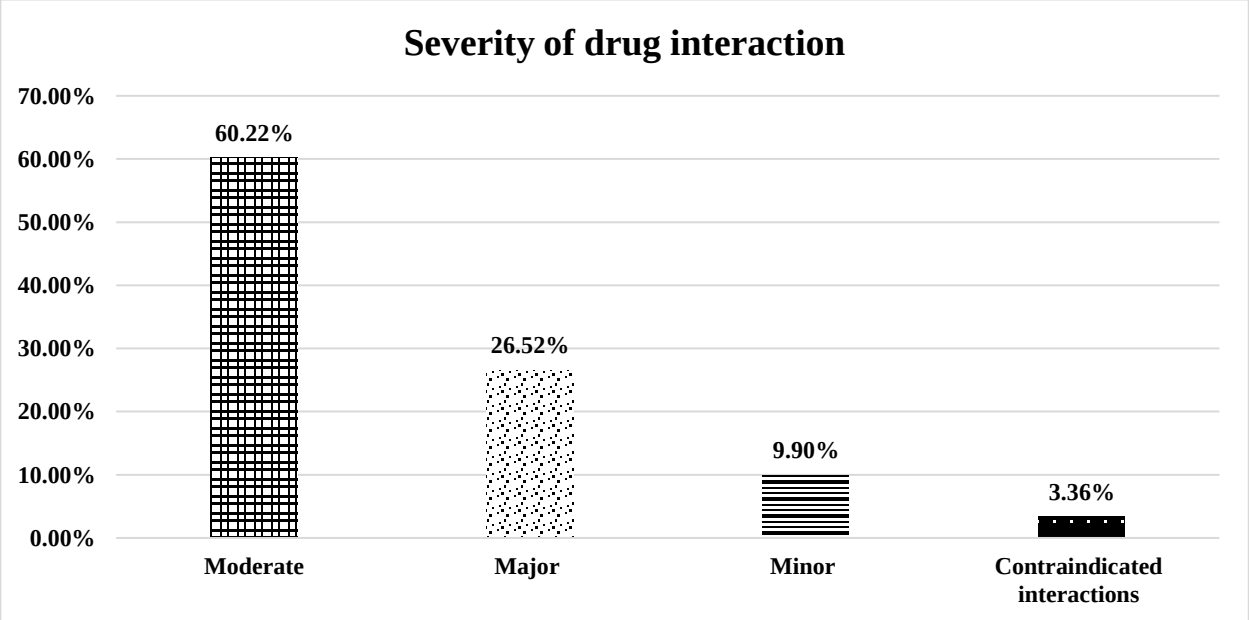

Figure 11. Severity of drug interaction

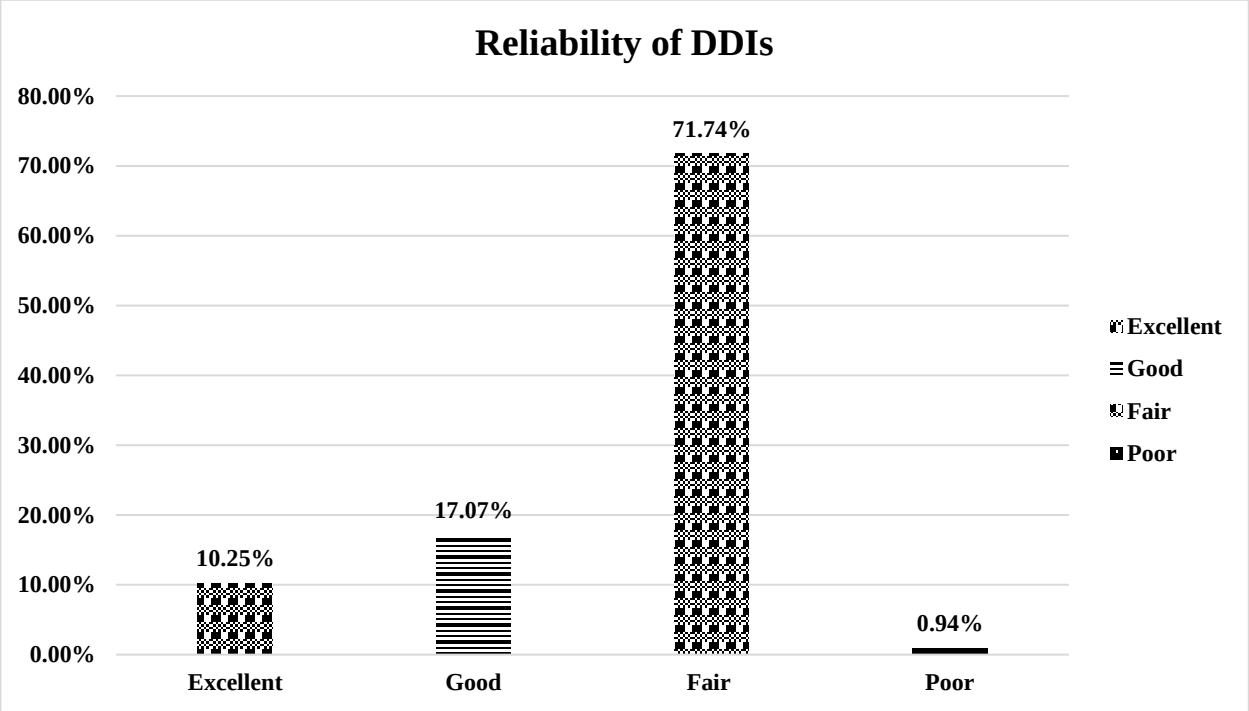

Figure 12. Reliability of DDIs

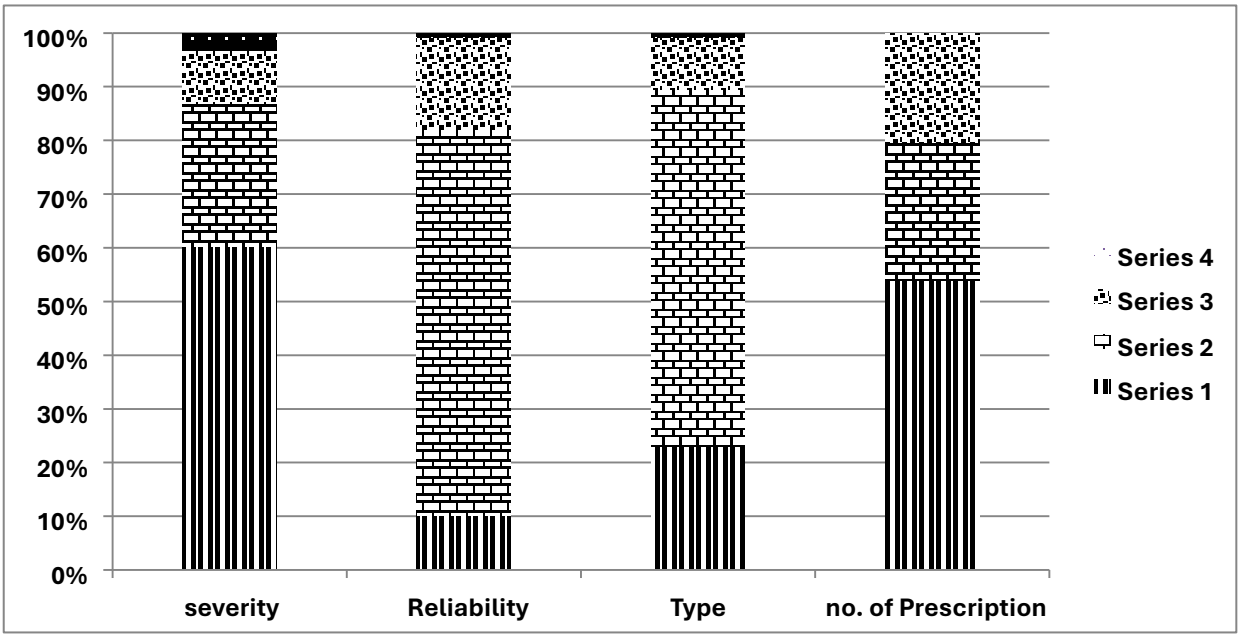

Figure 13. Comparison B/w different type of Interactions

Comparison B/w different type of Interactions

From above results and observations, pDDIs ratio is extremely high in certain areas of Pakistan. Similarly, polypharmacy in Diabetes, HTN and concomitant diseases leads to appearance of Adverse Drugs Events in maximum population like fainting, diabetes, hypoglycaemia, fatigue, fluid retention, Polyuria, glycosuria, hypotension, sexual dysfunctionality, Cataract formation and others respectively which disturbs patients' quality of life. Performed Review of prescriptions have showed that maximum no. of Potential Drug interactions is of category C with major to moderate severity and its reliability is fair to excellent. All these results and potential DDIs have also been confirmed by interviewing a number of patients which explained that they suffered above mentioned adverse drug reaction maximum times after taken up of their medication therapy. Similarly, appearances of Class D-type interactions though are less in number, but its severity and reliability are maximum. ADE

appeared because D-type interactions have distracted patients' quality of life to extreme limit. That's why after monitoring therapy if patients suffer these interactions, it required therapy modification which may be a change in therapy. Common interacting drugs found are Insulin, NPH, Regular, Metformin, sitagliptin, atorvastatin, furosemide, metoprolol, Indapamide, gabapentine, Tramadol, Alprazolam, Pregabaline, Ciprofloxacin, Bromazepam, niacinamide, pyrazinamide, hydrochlorthiazide, Diltiazem, Enalapril and Clopidogrel. Lexicomp have also indicated wrong practice in prescribing pattern high lighting some contraindicated combinations of drug. Common drug is orphenadrine, pregabaline, Diazepam, tramadol, alprazolam, Rifampicin, ipratropium etc. Some most common reported pDDIs which have also assessed by project fellows are as fellows.

Table 6. Interaction of Drugs

Drug 1	Interacting Drugs	Type of interaction
Insulin (NPH+Regular)	Metformin,sitagliptin,Empagliflozin,vildagliptin,furosemide, metoprolol	D
Aspirin	Clopidogrel,sitagliptin,insulin,Empagliflozin,Dapagliflozin Furosemide,ciprofloxacin,pyrazinamide,Dilitiazem,Enalapril	D &C
Sitagliptin+Metformin	metformin, Glimpiride, Atorvastatin,,Indapamide,Tramadol	C
Gabapentin	Tramadol	D
Tramadol	Alprazolam,Pregabaline,Aspirin,bromazepam	C
Niacinamide	Rosuvastatin	D
Diclofenac	Aspirin, Escitalopram, Hydrochlorothiazide, Prednisolone	D
Cimetidine	Amlodipine,Valsarta	D
Dilitiazem	Aspirin, atorvastatin	D
Naproxen	Escitalopram	D
Orphanedrine + Paracetamol	Diazepam, Tramadol, Alprazolam, Ipratropium	X
Esomeprazole	Rifampicin, INH, Pyrazinamide	X
Orphanadrine	Pregabaline	X

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