



# **Evaluation of Potential Drug-Drug Interactions among Patients of the Nephrology and Kidney Transplant Wards of a Major Teaching Hospital in Iran**

**Shahriyar Shahbazi Khamas<sup>1</sup>, Mohammadkazem Lebadi<sup>2</sup>, Asieh Ashouri<sup>3</sup>,  
Gholamreza Mokhtari<sup>2</sup> and Atefeh Jafari<sup>4\*</sup>**

<sup>1</sup>*School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran.*

<sup>2</sup>*Razi Clinical Research Development Center, Guilan University of Medical Sciences, Rasht, Iran.*

<sup>3</sup>*Department of Health Education and Promotion, Health and Environment Research Center, Faculty of Health, Guilan University of Medical Sciences, Rasht, Iran.*

<sup>4</sup>*Department of Clinical Pharmacy, School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran.*

## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author SSK data gathering, writing original draft, review and editing. Author ML, conceptualization author GM, guideline implementation, review and editing. Author AJ methodology, conceptualization, guideline implementation, writing original draft, review and editing. Author AA software, formal analysis. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Aims:** This study was aimed to find the prevalence of potential DDIs in patients and identify factors associated with these interactions.

**Study design:** All patients' medication regimens were screened for potential DDIs through Lexi-Interact® Online application.

\*Corresponding author: E-mail: [atf.jafari@gmail.com](mailto:atf.jafari@gmail.com);

**Place and Duration of Study:** This study was conducted for five months in 2017-2018 at the nephrology and kidney transplant ward of Razi hospital, Rasht, Iran.

**Methodology:** Each potential DDI was characterized based on severity, onset, mechanism, risk rating and reliability rating. The patient's comorbidity was assessed with the Charlson comorbidity index. The quality of patients' life was assessed with the Kidney Disease Quality of Life Instrument-SF36™ questionnaire.

**Results:** The study included 191 patients (109 [57.07%] males and 82 [42.93%] females) with a mean age of 58.09 ± 17.76 years. The analysis revealed that 29.4 % of potential DDIs had good and 13.5% had excellent evidence. There was a statistically significant association among the number of prescribed medications (polypharmacy), hospital ward, age, Body Mass Index, education, history of drug addiction, length of hospitalization, dyslipidemia, and hypothyroidism.

**Conclusion** Potential DDIs are common in patients of the nephrology and kidney transplant wards, so proper patient monitoring is essential for minimizing and preventing potential adverse outcomes of DDIs.

*Keywords: Nephrology; polypharmacy; drug interaction; chronic kidney failure.*

## 1. INTRODUCTION

Drug-drug interaction (DDI) can be defined as a noticeably harmful or beneficial process whereby the pharmacological consequence of a drug is directly or indirectly influenced and altered by the presence of another drug [1]. DDIs are a major clinical problem, accounting for 2–6% of all hospital admissions, of whom 1-2% having life-threatening circumstances [2]. The incidence of potential DDIs (pDDIs) in different countries varies from 6% to 99% due to variability in methodologies and settings, while in Iran, the median incidence of pDDIs was 19.2%[3].

The prevalence of chronic kidney disease (CKD) among the Iranian population is about 15% [4], and it is definitely a public health threat. CKD patients receive many medications (polypharmacy) to treat the underlying diseases leading to CKD or the common complications of CKD [5]. Patients with CKD and kidney transplantation are at high risk for adverse drug events (ADEs) such as drug interactions, nephrotoxic medications, and inappropriate drug dosing because they are frequently prescribed numerous medications. Besides, these ADEs can accelerate the loss of kidney function and may increase the risk of end-stage renal disease (ESRD); other consequences of ADEs are acute kidney injury (AKI) and prolonged hospitalization [6].

DDIs and their harmful consequences, such as increased morbidity, mortality, length of hospital stay, and healthcare costs in CKD patients, are preventable because of their predictable nature. DDIs can be prevented, or their progression can be delayed by identifying the patients with CKD and providing appropriate management. An easy

way to overcome DDIs is changing interacting drug to a non-interacting alternative. However, this is not always an option.

This study aimed to evaluate the prevalence and distribution pattern of pDDIs in patients admitted to the nephrology and kidney transplant wards and identify factors associated with these interactions if present.

## 2. MATERIALS AND METHODS

This study was a prospective observational cross-sectional study, carried out in nephrology and kidney transplant wards of Razi Hospital, a Middle Eastern referral hospital affiliated to Guilan University of Medical Sciences, Rasht, Iran, over five months between September 2017 and February 2018. All patients older than 14 years admitted to nephrology or kidney transplant wards of Razi hospital who at least received two medications and agreed to participate took part in this study.

The sample size was determined using a formula for estimating a single population proportion [7] with the assumption of 95% confidence level, the margin of error of 5%, and the prevalence rate of pDDI was 50%.

$$n = (Z_{\alpha/2})^2 \times p(1 - p) / d^2, n = (1.96)^2 \times 0.5(1 - 0.5) / (0.05)^2 = 384$$

The required number of prescriptions was 384. Considering reviewing patients' records at least three times, no less than 128 patients were required to be examined in accordance with the study protocol.

Where, d = marginal error, p = proportion of sample population with confidence interval of

95%,  $Z_{\alpha/2}$  = the value under standard normal table for the given value of confidence interval,  $n$  = sample size.

Data was collected using a data-gathering sheet designed for the study. Demographic (such as gender and age) and clinical data such as length of hospital stay, CKD stage, list of comorbidities, and the list of prescribed medications were collected. To perform additional analyzes and to find other possible risk factors, patient's comorbidities and quality of life were measured using the Charlson Comorbidity Index (CCI) [8] and Kidney Disease Quality of Life Instrument (KDQOL-SF36) [9] respectively.

Finally, all prescribed medications contained in the patient's records were collected at the time of admission and during the hospitalization period. During hospitalization, the medical records were reviewed at least three times at the appropriate intervals and eventually at the time of the patient's discharge or day of demise.

PDDIs among patient's medications in this study were evaluated through the online database Lexi-Interact®. According to various studies, this software's accuracy is 87% -100%, and its specificity is 80-90%, which makes these features a highly validating interaction screening program [10]. In this study, the pharmaceutical interactions and drug interactions with food or complementary herbal products were not investigated.

Categorical variables were expressed as a percentage, and continuous variables were reported as mean  $\pm$  SD. Logistic regression analysis was applied to identify the association of one or more DDIs with patients' clinical or demographic information. Initially, univariate logistic regression analysis was carried out. Then, for variables with significant univariate p-values, multivariate analysis were performed to identify risk factors associated with pDDIs. P-value  $<0.05$  was considered statistically significant. Statistical Package for the Social Sciences (SPSS) version 24 (SPSS Inc., Chicago, IL) was used for statistical analyses.

### 3. RESULTS AND DISCUSSION

During the study period, 191 patients who met the inclusion criteria were recruited in our study. Table 1 demonstrates the demographic and clinical characteristics of the patients. The average length of stay was  $13.88 \pm 8.76$  days.

Totally, 830 evaluations were performed at appropriate time intervals. The total number of drugs in 830 prescriptions were 6478. Calcium Carbonate (16.5%), Furosemide (6.8%), Carvedilol (6.2%), Insulin (6.1%), Amlodipine (5.9%) were the five most common drugs with the highest frequency of interactions (Table 1).

**Table 1. The most commonly used drugs with the highest frequency of interactions**

Drug	Number of DDIs
Calcium Carbonate	1073
Furosemide	445
Carvedilol	407
insulin	397
Amlodipine	383
Prednisolone	379
Glyceryl Trinitrate	345
Cyclosporine	320
Diltiazem	313
Atorvastatin	287
Hydrocortisone	261
Ciprofloxacin	249
Calcitriol	223
Ferrous Sulfate	217
Mycophenolate Mofetil	205
Aspirin	187
Pantoprazole	177
Tacrolimus	157
Tamsulosin	145
Prazosin	142
Captopril	129

A total number of 3957 pDDIs were identified among subjects while three patients had no known interaction; at least one pDDIs were observed in the prescribed drugs of the remaining patients. The average number of pDDIs for each patient was 16 (IQR = 9-27 and range 1 to 108 interactions) in total evaluations during the hospitalization period. 88.3% were of moderate severity, and 55.9% had fair evidence (Table 2).

Investigating the relationship between the demographic and clinical characteristics of patients with the number of pDDIs, based on the Kruskal Wallis test for qualitative variables and Spearman correlation coefficient test for quantitative variables showed a relationship with the hospitalization at transplant ward, age, Body Mass Index, education, history of drug addiction, number of medications, polypharmacy, length of hospitalization, dyslipidemia and hypothyroidism ( $P < 0.05$  for all cases) (Table 3).

**Table 2. Twenty most frequently identified DDIs and their levels**

No.	Interaction	Frequency	Severity	Risk Rating	Reliability rating	Mechanism	Onset
1	Calcium Carbonate + Amlodipine	196	Moderate	C	Excellent	Pharmacodynamics	Not specified
2	Calcium Carbonate + Calcitriol	126	Moderate	C	Fair	Pharmacodynamics	Not specified
3	Prednisolone + Calcium Carbonate	109	Moderate	D	Good	Pharmacokinetic	Not specified
4	Ferrous Sulfate + Calcium Carbonate	106	Minor	D	Good	Pharmacokinetic	delayed
5	Glyceryl Trinitrate + Furosemide	106	Moderate	C	Fair	Pharmacokinetic	Not specified
6	Insulin + Insulin	88	Moderate	C	Fair	Pharmacodynamics	Not specified
7	Carvedilol + Atorvastatin	84	Moderate	C	Fair	Pharmacokinetic	Not specified
8	Pantoprazole + Ferrous Sulfate	77	Moderate	C	Good	Pharmacokinetic	Rapid
9	Hydrocortisone + Calcium Carbonate	75	Moderate	D	Fair	Pharmacokinetic	Not specified
10	Ciprofloxacin + Calcium Carbonate	73	Moderate	D	Excellent	Pharmacokinetic	Rapid
11	Glyceryl Trinitrate + Carvedilol	73	Moderate	C	Fair	Pharmacodynamics	Not specified
12	Mycophenolate Mofetil + Calcium Carbonate	71	Moderate	D	Good	Pharmacokinetic	Not specified
13	Calcium Carbonate + Atorvastatin	65	Minor	C	Fair	Pharmacokinetic	Not specified
14	Prazosin + Carvedilol	53	Moderate	C	Fair	Pharmacodynamics	Rapid
15	Calcium Carbonate + Allopurinol	52	Moderate	D	Good	Pharmacokinetic	Not specified
16	Captopril + Calcium Carbonate	52	Moderate	C	Fair	Pharmacokinetic	Rapid
17	Diltiazem + Calcium Carbonate	52	Moderate	C	Excellent	Pharmacodynamics	Not specified
18	Pantoprazole + Mycophenolate Mofetil	56	Moderate	C	Good	Pharmacokinetic	Rapid
19	Prednisolone + Furosemide	48	Moderate	C	Good	Pharmacodynamics	Not specified
20	Tacrolimus + Prednisolone	48	Moderate	C	Fair	Pharmacokinetic	Not specified

**Table 3. Demographic and clinical characteristics of the study population and their relation to drug-drug interactions**

	<b>Number (%)</b>	<b>p-value</b>
Ward	Nephrology	146 (76.4)
	Kidney transplant	45 (23.6)
Gender	Male	109 (57.07)
	Female	82 (42.93)
Age	<45	41 (21.46)
	45-60	56 (29.32)
	60-75	55 (28.8)
	>75	39 (20.42)
Body Mass index	Underweight	40 (20.9)
	Normal	68 (35.6)
	Overweight	49 (25.7)
	Obese	34 (17.8)
Underlying Renal Disease	Hypertension	128 (67.01)
	Diabetes mellitus	28 (14.66)
	Lupus Nephritis	6 (3.14)
	<i>Glomerulonephritis</i>	3 (1.57)
	Infection	1 (0.52)
	Unspecified	25 (13.1)
Comorbidity	Hypertension	152 (79.58)
	Diabetes mellitus	72 (37.7)
	Dyslipidemia	58 (30.36)
	Ischemic heart disease	25 (13.09)
	Benign prostate hyperplasia	19 (9.95)
	Hypothyroidism	11 (5.76)
	Systematic lupus	6 (3.14)
	Alzheimer	3 (1.6)
	Rheumatoid arthritis	2 (1.05)
	Asthma	2 (1.05)
	Chronic heart failure	1 (0.52)
	Disposition	Death
Discharge		180 (94.24)
Transfer to another hospital		5 (2.62)

Charlson comorbidity index	Low (0 points)	5 (2.62)	0.026
	Medium (1-2 points)	33 (17.28)	(Correlation: -0.161)
	High (3-4 points)	68 (35.6)	
	Very high (≥5 points)	85 (44.5)	
Level of Education	Under diploma	15 (7.8)	0.000
	Diploma	53 (27.8)	(Correlation: 0.396)
	Bachelor	15 (7.8)	
	Master	1 (0.52)	
	PhD	1 (0.52)	
	Not educated	102 (53.04)	
	Not specified	4 (2.09)	
Pattern of Renal Disease	Acute kidney disease (AKI)	37 (19.5)	0.157
	Chronic kidney disease (CKD)	97 (51)	
	AKI on CKD	56 (29.5)	
Chronic kidney disease Stage	2	10 (5.2)	0.179
	3a	14 (7.3)	(Correlation: 0.098)
	3b	16 (8.4)	
	4	66 (34.7)	
	5	84 (44.2)	
Kidney disease quality of life instrument- SF36™ Physical health components summary	<40	2 (3)	0.201
	40-60	42 (62.7)	(Correlation: -0.158)
	60-80	21 (31.3)	
	80-100	2 (3)	
Kidney disease quality of life instrument - SF36™ Mental health components summary	<40	1 (1.5)	0.471
	40-60	25 (37.3)	(Correlation:- 0.09)
	60-80	38 (56.7)	
	80-100	3 (4.5)	
Kidney disease quality of life instrument - SF36™ Kidney disease components summary	40-60	38 (56.7)	0.287
	60-80	24 (35.8)	(Correlation: -0.132)
	80-100	5 (7.5)	
Kidney disease quality of life instrument - SF36™ total	40-60	37 (55.2)	0.266
	60-80	27 (40.3)	(Correlation: 0.138)
	80-100	3 (4.5)	

**Table 4. Severity, Mechanism, Onset, Reliability Rating and Risk Rating of detected potential drug-drug interactions**

Severity	Minor	188 (4.8)
	Moderate	3495 (88.3)
	Major	274 (6.9)
Mechanism	Pharmacodynamics	2203 (60.3)
	Pharmacokinetics	1569 (39.7)
Onset	Rapid	621 (15.73)
	Delayed	624 (15.77)
	Unspecified	2712 (68.5)
Reliability Rating	Excellent	535 (13.5)
	Good	1164 (29.4)
	Fair	2213 (55.9)
	Poor	45 (1.2)
Risk Rating	C	2993 (75.65)
	D	903 (22.8)
	X	61 (1.55)

**Table 5. Frequency of drug-drug interactions based on patients characteristics**

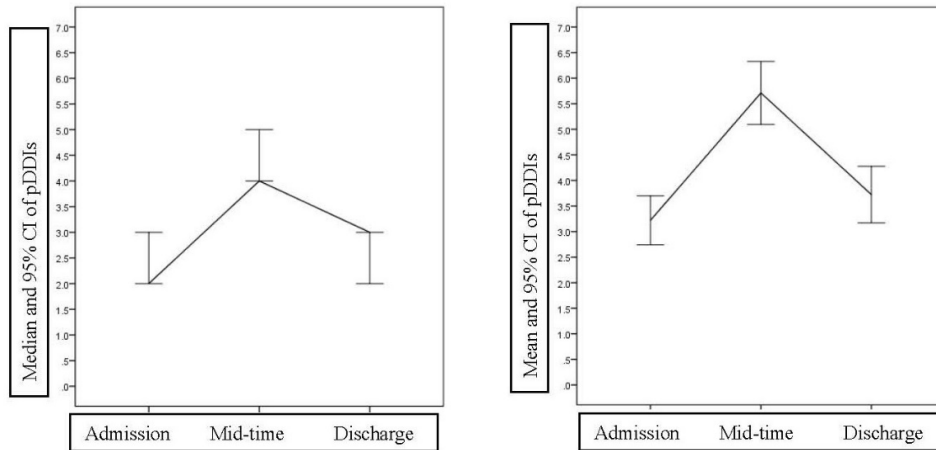
		Percentage	Mean number of pDDIs	Number of pDDIs (N=3957)
Chronic kidney disease stage	1	0.52	1.25	5
	2	5.23	5.35±4.66	199
	3a	7.33	4.89±2.94	288
	3b	8.38	4.65±4.15	336
	4	34.56	4.58±3.68	1314
	5	43.98	5.07±3.81	1811
Gender	Male	57.07	4.63±3.64	2111
	Female	42.93	5.14±3.91	1842
Age	<45	21.46	5.27±4.34	937
	45-60	29.32	6.42±3.73	1587
	60-75	28.8	4.25±3.64	954
	75>	20.42	3±1.98	475

Charlson comorbidity index	Low (0 points)	2.62	3.54±4.15	76
	Medium (1-2 points)	17.28	6.30±4.57	893
	High (3-4 points)	35.6	5.13±3.64	1499
	Very high (≥5 points)	44.5	4.13±3.32	1485
Kidney Disease Quality of Life Instrument-SF36™	≤60	58.21	6.93±4.168	1126
	≥60	41.79	6.82±5.2	899
Length of stay	≤10	48.17	4.26±3.09	1558
	≥10	51.83	5.39±4.22	2395

**Table 6. Regression coefficient and its significance in assessing the relationship between the demographic and clinical characteristics of the patients with the number of potential drug-drug interactions**

		Unstandardized Coefficients		Standardized Coefficients (Beta)	t	P-value	Adjusted R2
		B	Std. Error				
<b>Nephrology Ward (n=146)</b>							
<b>Model 1</b>	(Constant)	0.732	0.756		0.968	0.335	0.468
	Total number of medications	0.139	0.016	0.569	8.529	<0.001	
	Hypothyroidism	2.709	0.891	0.203	3.041	0.003	
	Age category	-0.506	0.190	-0.168	-2.669	0.009	
<b>Model 2</b>	(Constant)	1.882	1.149		1.638	0.104	0.236
	Hypothyroidism	5.361	0.973	0.401	5.512	0.000	
	Stage of chronic kidney disease	0.722	0.213	0.255	3.394	0.001	
	Age category	-0.739	0.225	-0.246	-3.278	0.001	
<b>Transplant Ward (n=45)</b>							
<b>Model 1</b>	(Constant)	0.999	1.538		0.650	0.520	0.365
	Total number of medications	0.168	0.035	0.618	4.784	<0.001	
<b>Model 2</b>	(Constant)	5.613	1.147		4.893	<0.001	0.110
	Length of stay	0.150	0.063	0.366	2.391	0.022	





**Fig. 1. Trend of potential drug-drug interactions during hospitalization**

In the transplant ward, the results of the multiple regression analyses showed that only the higher number of medications during hospitalization was related to more pDDIs per day. Because of the strong relationship between the number of medications and potential DDIs per day, which may mask the relation of other variables with potential DDIs, the analysis was performed again after removing the number of medications variable. In the second analysis, the length of stay remained as an independent predictor in the model (beta=0.15, 95%CI: 1.55-3.12, P<0.001) (Table 4). The length of hospitalization explained only 11% of the potential DDIs variation.

In the nephrology ward, multiple regression analysis of pDDIs per day were independently associated with the number of medications, hypothyroidism, and patient's age group (Table 4). After removing the number of medications variable, hypothyroidism, age group, and stage of CKD were entered into the model in the second analysis. Variation of these variables explained 24% of the potential DDIs variation. Thus, more number of medications (polypharmacy), hypothyroidism, lower age group, and higher CKD stage were independently related to the more potential DDIs per day in the nephrology ward patients.

Fig. 1 shows the trend of interactions during hospitalization. The number of DDIs in admission (mean 3.22, median 2) increased during hospitalization (mean 5.71, median 4) and decreased at the time of discharge (mean 3.72, median 3); this shows patients during hospitalization are at increasing risk of pDDIs and the decreasing trend toward discharge may

be due to mid-day discharge and patients not receiving all of their medications that may interact.

The prevalence of DDIs in hospitalized patients is one of the major problems in the treatment system. More monitoring is needed to minimize the adverse effects of drugs, improve the quality of life and reduce complications, deaths, and costs associated with DDIs [11]. DDIs, can potentially complicate the nature and severity of an illness such as CKD that requires multiple and complex therapeutic regimens [12]. Compared with other studies conducted in the nephrology ward, this study showed a higher incidence of pDDIs (98.4%). The prevalence of DDIs in CKD patients of three different studies was 89.1% [13] 76.09% [14] and 78% [15]. Differences in trial design, methodology, DDI definitions and approaches to screening, the pattern of drug prescribing, the difference in sensitivity and specificity of various software, study setting, and special conditions of the studied population could account for the difference in the prevalence rates of pDDIs in the different studies. All of these make it difficult to compare studies with each other. Many of the pDDIs can be avoided with close patient monitoring or the use of alternative therapeutic agents, and omission of unnecessary medications. However, it may be challenging for physicians to recall the multiple DDIs and their clinical significance. Clinical pharmacists can play a role in the identification and monitoring of pDDIs [16,17]. The relatively high prevalence of DDIs in this hospital is perhaps due to the lack of facilities, the absence of DDIs screening programs, and the shortage of clinical pharmacists.

The severity of pDDIs is one of the main factors to be considered for proper evaluation and management of pDDIs. Therefore, health care providers need to identify and classify pDDIs properly. The majority of the interactions were of moderate severity. It is crucial for the clinical management of pDDIs, minimizing their risk, and designing prophylactic measures for prevention. This is similar to Fasipe et al., in which moderate severity was about 67% [15]. Regarding the risk rating, Type C interactions accounted for most of the interactions, similar to previous studies ([13,18] It is recommended that an appropriate monitoring plan should be implemented to identify potential negative effects and avoid probable complications.

The reliability rating for more than half of the pDDIs (55.9%) was fair; this was similar to Khan et al. in which the majority of the pDDIs were fair in reliability [19] Our findings show about half of pDDIs have a theoretical basis for inferring the possibility of an ADE, but these interactions have not been substantiated in clinical practice. However, the importance of pDDIs with fair or poor documentation should not be ignored and should be evaluated by a specialist because they may result in severe consequences in the case of potentiation by similar interactions or predisposing risk factors.

Most of the DDIs had unspecified onset. Of the remaining, about 16 % were delayed onset, if an interaction occurs during hospitalizations, it may not manifest itself immediately, and if interacting drugs are to be continued for the patient on an outpatients basis, then this could potentially result in decreased efficacy of drugs leading to therapeutic failures and potential ADEs, so these interactions would require long-time follow-up in order to determine the clinically significant outcome of these interactions. A total of 15.7% of DDIs were rapid; rapid DDIs are expected to occur within 24 hours of drug consumption. As is clear, rapid DDIs require instant intervention, which will not be achieved unless the pharmacist attends medical rounds. Rama et al. reported that 50% of DDI were of delayed onset and 39% were of rapid onset [14]

The mean number of drugs prescribed to patients during hospitalization was about eight, similar to Guastaldi et al. [20] Drugs involved in most pDDI were those commonly used in the treatment of hypertension. Mineral supplements such as calcium carbonate and ferrous sulfate played an important role in DDIs. Patients with

polypharmacy were found to have a higher rate of exposure to pDDIs; this is because a higher number of simultaneous medications increases each drug's probability of potential interaction with another drug [21] The practice of polypharmacy in managing of CKD patients is not unexpected because they have a high number of cardiovascular risk factors, comorbidities, and complications managed by a combination of drugs.

The findings of this study showed there was a significant association between hospitalization in the kidney transplant ward and exposure to DDIs; this can be explained as patients in the kidney transplant ward receive more drugs on average, often including calcineurin inhibitors (CNIs), antimetabolites, anti-infectives, statins, and antihypertensive drugs. On the other hand, they receive prophylactic treatments, and the most important issue is the type of medication they receive.

Prolonged hospitalization may increase the total number of drugs consumed in the entire course of hospitalization. Prolonged hospitalization in this study was significantly associated with a higher number of DDIs, which is similar to another study by Moura et al. [22] Prolonged hospitalization indirectly increases the chance of DDIs [23] through the increased number of prescribed drugs; as mentioned earlier, there is a strong relation between polypharmacy and DDIs and, consequently, hospitalization.

The most common comorbidities in this study were hypertension and diabetes, respectively, which agreed with previous studies [15]; this can be attributed to the fact that both diseases are the leading etiologies of CKD worldwide. Each comorbidity needs its medication treatment, leading to polypharmacy, high drug burden, and occurrence of DDIs. Among comorbidities, hypothyroidism and dyslipidemia increased the rate of pDDIs in this study significantly. Levothyroxine is the drug of first choice for hypothyroidism and interacts with a wide range of medications such as proton-pump inhibitors (PPIs), antacids, iron salts, calcium, and phosphorus salts, as evident in this study [24] Hypothyroidism in ESRD patients is high [25], so this comorbidity needs more attention in the nephrology department. Dyslipidemia can affect kidney function and significantly increases the risk of cardiovascular disease development [26] Lipid-lowering drugs have both pharmacokinetics and pharmacodynamics interactions with a vast

group of drugs, increasing the risk of myotoxicity in patients. Transplant patients are at high risk of DDIs and myotoxicity due to the use of CNIs. Of drugs used in this study, cyclosporine and gemfibrozil require more attention owing to the high risk of DDIs.

According to previous studies, patients with lower CCI experience less premature death or graft loss, Therefore, in general, patients who undergo kidney transplant surgery should have lower CCI. For this matter, the relationship between CCI and the incidence of DDIs was evaluated separately for the patients in the nephrology and kidney transplant ward. In this study, the mean overall CCI score in both wards was  $4.24 \pm 1.89$ , and there was no significant relationship between CCI and DDIs.

Gencer et al. previously reported the number of drugs used (polypharmacy) influenced the quality of life [27] so in this study, we investigated the relationship between KDQOL and exposure to DDIs. Unfortunately, due to the small number of people who answered the KDQOL questionnaire (67 patients), a significant relationship between KDQOL and any of its physical, mental, and kidney disease domains with pDDIs was not found.

The majority of the patients with stage G4 and G5 had the highest prevalence of the pDDIs, probably because the early stage of CKD is usually asymptomatic; thereby, they refer to the hospital when the disease has worsened to the later stages with symptoms. In the later stages of the disease, patients with renal insufficiency are at higher risk of pDDIs [28] It should be kept in mind that drug-screening softwares deliver only immediate computerized drug interaction contents, which should be evaluated cautiously by the clinical pharmacists. To recognize pDDIs carefully, clinicians should consult pharmacists while prescribing drugs to CKD patients and seek their knowledge to avoid over or underestimating the clinical relevancy of pDDIs.

The results of this study confirm that medication-related problems, such as DDIs, exist beyond polypharmacy. There are several solutions to the incidence of DDIs, setting up a computerized screening program [22] participation and involvement of pharmacists, especially clinical pharmacists in the treatment process [29] setting up clinical decision support software, improving knowledge of health care professionals, and most important of all require medication

reconciliation both on admission as well as at discharge for all patients by trained pharmacists.

#### **4. CONCLUSION**

Potential DDIs are common in patients of nephrology and kidney transplant wards, so proper patient monitoring is essential for minimizing and preventing potential adverse outcomes of drug-drug interactions. Hospital or clinical pharmacists can play a critical role in improving treatment and reducing hospitalized patients' drug-related problems. Implementing the process of drug reconciliation by a trained pharmacist is recommended in order to detect DDIs as early as possible and minimize therapeutic failure and ADEs.

#### **5. STRENGTH**

Each patient was checked several times, and the incidence of interactions was monitored from admission to discharge. It is likely to be the first study to determine the association between a patient's quality of life and DDIs.

#### **6. LIMITATIONS**

The results of this study may provide baseline data that can be applied in finding the prevalence of pDDIs in patients of the nephrology and kidney transplant wards and identify factors related to these interactions which can aid in designing and implementing appropriate interventions, educational programs, and carrying out other related studies. All DDIs reported here were mainly potential; the presence of potential interactions does not always mean that the interactions actually occurred in the patients. Clinical outcomes of the patients related to DDIs were not followed in this study. This study encountered several limitations, including a limited sample size and a short-term frame. In addition, the findings of this study may not be generalized, as it is a single-centre study. Despite these limitations, this study's findings can be useful as input for understanding the extent of the problem and taking measures to improve the practice of managing drug interactions.

#### **DISCLAIMER**

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely

no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

## ETHICAL APPROVAL

The study protocol was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1397.011), and the privacy of the patients was assured.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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