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PROSPECTIVE EVALUATION OF DRUG PRESCRIBING AND IMPROVEMENT OF DRUG SAFETY IN RENAL FAILURE PATIENTS

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ABSTRACT

***Plan*:** *To assess the incidence of inappropriate dosing of renally excreted drugs in hospitalized patients with renal impairment.*
Preface: *Inappropriate dosing in patients with renal dysfunction can cause drug accumulation and toxicity.*
Method: *Creatinine clearance or estimated glomerular filtration rate of patients with serum creatinine greater than 1.7 mg% was calculated using Cockroft-Gault equation and Modified Diet in Renal Disease equation respectively. Dose of all potentially nephrotoxic drugs was evaluated using the published drug dosing guidelines and the new dose or dosing interval was recommended based on the patient's individual degree of renal impairment.*
Outcome: *Five hundred and six drugs in 50 patients were evaluated of which the dosages of 88 (17.39%) drugs were not adjusted at the time of prescribing. Most of the drugs requiring dose adjustment were antibiotics (39.77%) and antihypertensives (14.77%). About 27% of the drugs were to be avoided strictly.*
Conclusion: *Drug dosing evaluation and concurrent feedback mechanism by the pharmacist improve drug safety in patients with renal impairment.*

1. INTRODUCTION

Kidney disease is a common, progressive illness that is becoming a global public health problem. Indeed, the incidence of *Chronic Kidney Disease* (CKD) is increasing alarmingly in most industrialized countries. The prevalence of CKD among the Indian adult population was recently estimated to be > 13% (>25 million adults), and the number of patients with ESRD alone has risen from 209,000 in 1991 to 472,000 in 2004 whereas glomerulonephritis was one of the leading causes of kidney disease several decades ago. Kidney disease rank third amongst life threatening diseases after cancer and cardiac ailments[1]. Chronic kidney disease can affect glomerular blood flow, filtration, tubular secretion, reabsorption, renal bio-activation and metabolism.

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Drug absorption, bioavailability, protein binding, volume of distribution, and non-renal clearance (metabolism) can also be altered in these patients.[2]

A dose adjustment in renal failure is especially critical because parent compounds or active metabolites can accumulate and cause additional morbidity and costs. The adjustment of drug dosage to individual patient requirements can maximize therapeutic efficacy and minimize the adverse drug reactions.

The need for appropriate dose reduction in patients with renal failure is illustrated by earlier studies in which ranitidine-associated central nervous system (CNS) adverse drug reaction occurred more frequently in patients with renal impairment and the incidence of imipenem/cilastatin – associated seizures was reduced after dosage adjustment to renal function.[3] Munepa et al.[4] reported 37.6% of potential dosing errors in the drugs prescribed for azotemic patients in the medical wards of KholKaen hospital Thailand. Literature reveals that only few studies have assessed drug prescriptions and dosage adjustments in renal impairment.[3] The GFR which is most frequently estimated by using the equation Cockroft- Gault that incorporates serum creatinine concentration along with demographic data is the most commonly used index of overall kidney function.

Renal dysfunction affects more than just the renal clearance of drugs and /or active metabolites. A general guideline for administering drugs to patients with renal dysfunction is that when *fe* (fraction of the drug excreted unchanged in the urine) is >0.3, a dosage adjustment is most likely required at least in patients with severe renal impairment ($CrCl<30$ mL min^{-1}). Also, patients with chronic renal failure have serious health problems and require multiple medications. Obviously, extra cautions warranted when prescribing drugs with narrow therapeutic index.[1]

Many drugs which are prescribed to renal impaired patients like cephalosporins, aminoglycosides, fluroquinolones, beta-blockers, diuretics and hypoglycemic agents are eliminated primarily unchanged through the renal route. These drugs will create complications due to drug accumulation and should be adjusted to optimize the therapy. Dose adjustment in renal impairment can easily be achieved by estimating creatinine clearance based on serum creatinine; and adjusting dose and/or dose interval. Dose adjustment in patients with renal failure reduce both the cost of the drug therapy and the risk of adverse drug reaction.[3] The aim of the study was to understand the prescribing pattern in patients with renal impairment, to assess the incidence of inappropriate dosing of renally excreted drugs and also to perform drug dosage adjustments for all potentially nephrotoxic or renally excreted drugs.

2. METHODOLOGY

A prospective descriptive study was carried out in the General Medicine department of a 700 bedded multispecialty tertiary care teaching hospital for a period of 6 months (March – August 2013).Patients who were admitted in general medicine department, prescribed with at least one pharmacologically active drug and who had at least one estimated serum creatinine value more than 1.7mg/dL (Normal range: 0.8 – 1.2 mg/dL) [5] were included in the study.

Patients who were undergoing dialysis, not willing to participate in study and whose medical record showed insufficient data were excluded from the study. Major outcome measure was the number or percentage of drug dosage regimens adjusted to renal function.

The study protocol was approved by institutional review board. Patients with impaired renal function were identified based on laboratory data and clinical evaluation. Verbal consent was obtained from each subject before initiating the study. Various clinical and demographic details of the patients such as age, gender, body weight, length of hospital stay, primary diagnosis, serum urea and creatinine levels were collected using structured proforma. Treatment data including prescribed drugs, dosages, frequency and route of administration were also recorded.

For all prescribed drugs, the fraction of the bioavailable dose which is eliminated extra-renally (Q_0) was obtained from literature. Dose adjustments was considered mandatory if at least 70% of bioavailable, active form of drug is eliminated by the kidney in unchanged form ($Q_0 \leq 0.3$) or potential nephrotoxicity is previously documented in the literature.

Creatinine clearance was calculated by using Cockroft-Gault equation.[6]

$$CrCl = \frac{(140 - age) \times Weight\ in\ kg}{Serum\ Creatinine\ \times 72}$$

Instead of creatinine clearance, GFR was calculated by using Modification of Diet in Renal Disease (MDRD) formula whenever patient's weight was not available.[5]

$$GFR = 186.3 \times (Serum\ creatinine)^{-1.154} \times (Age)^{-0.203} \times 0.742\ (Female)$$

For obese patients, the dosing weight was calculated[7] before calculating creatinine clearance by Cockroft-Gault equation.

$$IBW\ for\ male\ patients = [Height\ (cm) - 80] \times 0.7$$
$$IBW\ for\ female\ patients = [Height\ (cm) - 70] \times 0.6$$
$$Dosing\ Weight = (ABW - IBW) \times 0.4 + IBW$$

Creatinine clearance, eGFR and Ideal Body Weight (IBW) were calculated using Micromedex software. [6] After determining the degree of renal insufficiency the patients were grouped according to their stages of renal impairment as recommended by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) [7] and Food& Drug Administration (FDA) [8].

Stage	*Description*	*e GFR(mL/min/1.73m^2)*	*CrCl(mL/min*
1	Control (normal)	≥ 90	≥ 90
2	Mild decrease in GFR	60 – 89	60 - 89
3	Moderate decrease in GFR	30 – 59	30 – 59
4	Severe decrease in GFR	15 – 29	15 – 29
5	End Stage Renal Disease (ESRD)	<15 not on dialysis Requiring dialysis	<15 not on dialysis Requiring dialysis

After estimating creatinine clearance the dose of the medication of interest was then evaluated using the published drug dosing guidelines for the patient's individual degree of renal impairment.[6,9,10.]

Each medication was then categorized as either 'dose adjusted' if its dosing was found within the target range or 'dose not adjusted' if the prescribed dose exceeded the relevant dose threshold.

When necessary, the new dosages or dosing intervals were accurately estimated by using the following formula[8]

$$New\ Dose = \frac{Patient's\ CrCl \times Normal\ Dose}{Normal\ CrCl}$$

$$New\ Dosing\ Interval = \frac{Normal\ CrCl \times Normal\ Dosing\ Interval}{Patient's\ CrCl}$$

For patients whose follow up serum creatinine was determined, creatinine clearance was estimated and dose requirements were calculated once again.

RESULTS

A total of 506 drugs in 50 patients were evaluated in the present study with a mean of 10.88 ± 3.36 drugs per patient. The mean age of the study population was 58.46± 12.75(range 32 to 86yrs) with 74% male patients. Their mean serum creatinine level was 5.48 mg% ± 3.04 (range 1.7 to 15.2 mg/dl) and mean creatinine clearance was 15.51mg/ml ± 10.05 (range 4.21 to 44.2 ml min^{-1}). Demographic details of these patients are shown in **Table 1**. Most of the patients (52%) were in the late adulthood (51-65yrs). The major diagnoses were renal failure (96.0%), hypertension (58.0%) and diabetes mellitus (34%). About 84% of patients had multiple co-morbidities. The stages of renal impairment of the selected subjects are shown **Table 2.**

It was found that 17.59% of the prescribed drugs were renally eliminated with at least 70% of the drugs in unchanged form (ie. Q_0<0.3) or potentially nephrotoxic. On an average each patient with renal dysfunction received about 2 renally eliminated drug (Q_0<0.3) or nephrotoxic drugs.

About 16% of patients were prescribed with 13 drugs each and 12.24% with 12 drugs each. **Figure 1** illustrated the number of drugs prescribed per patients. Vitamins and mineral supplements were most commonly prescribed (84%). The major drug category prescribed was antibiotics (13.04%), antihypertensives (11.07%) and antiulcer (9.29%) drugs. This is depicted in **Table 3.**

Among the 506 evaluated drugs, 107 (21.14%) required dose adjustments. Of these, dose of 19 (3.75%) were adjusted at the time of prescribing and 88 (17.39%) were not adjusted. The prescribed drugs with dosages not adjusted and those drugs with contraindications in renal impairment are detailed in **Table 4.**

Major types of errors identified were overdose (60.6%), and wrong frequency of administration (12.12%). About 27% of the drugs were to be avoided strictly in renal impairment as per the available evidences. (**Table 5**). Further, 94% of the patients needed dosage adjustment for at least one drug prescribed.

Seventy three (28.85%) prescribed drugs had drug-drug interactions. Of these 29 (37.9%) were major interactions and 4 (5.47%) combinations were contraindicated. (**Table 6**). Toresemide with ceftriaxone or pantoprazole was the most frequently identified interacting drug combinations. Interactions which can directly influence kidney function were also observed in 4 cases. These included Ceftriaxone with Calcium gluconate, Clopidogrel with Rabeprazole, and Eplerenone with Spironolactone

Prescriptions of 20% of the patients had either theophylline or prazosin, which are drugs with narrow therapeutic index. In patients with renal impairment the chance of accumulation of these drugs is of high alert.

DISCUSSION

Kidney plays vital physiological functions and it acts as the major excretory organ in the human body. Renal function can be assessed by various tests and procedures that will help evaluate the kidney function. Drug therapy in the presence of renal diseases requires to be individualised. Some drugs are to be avoided and some others may require dose adjustments in order to avoid drug toxicity.

The major test which can be performed to assess the renal function is the estimation of serum creatinine in urine as well as blood. Creatinine is a by-product of muscle metabolism in the body and it is primarily eliminated through glomerular filtration. Thus the accumulation of creatinine in blood indicates abnormal or diminished renal function.[11]

The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF KDOQI) advocates the use of creatinine clearance (CrCl) and estimated glomerular filtration rate (eGFR) for calculating the individualised dose. Once the CrCl or eGFR is estimated CKD is classified into five stages proposed by KDOQI and approved by FDA. Estimation of GFR is done with the help of Modification of Diet in Renal Disease (MDRD) equation and CrCl by Cockroft-Gault equation. [2]The Cockroft-Gault equation is still most often used for estimating GFR in pharmacokinetic studies and for drug dosage adjustments, although some studies have shown the MDRD equation to be more accurate for estimating GFR. [12]

The present study found that the dosages of 17.39% of drugs were not adjusted at the time of prescribing. Falconnier et al[4] reported 17% of inappropriate prescriptions which was comparable to the present study. A similar study [13] carried out in the nephrology department of the same study site showed only 7% inappropriateness. This may be due to the fact that the drugs were prescribed by nephrologists whereas in the present study patients with renal impairment were managed in the general practice or general medicine department. Moreover, multiple co-morbidities of the study population and polypharmacy were the major reasons to expose them to various categories of drugs which can easily lead to dosing errors.

The study revealed that most of the dosage errors were seen with antibiotic containing prescriptions followed by antihypertensives. The major drug categories for which drug dosage adjustments were recommended by the pharmacist based on the available evidence are discussed below.

Antibiotics

A CRF case with UTI was prescribed with amoxicillin 1g twice daily. But literature [6] reveals that in severe renal impairment the maximum tolerated dose of amoxicillin is 1g per day. If accumulation of this drug occurs common side effects like epigastric distress, crystalluria, nephritis etc. would aggravate and result in complications like oral thrush, vaginal yeast infection etc. Hence for this patient a reduced dose of 500mg BD/ 1g OD of amoxicillin or an alternate therapy with dose adjusted ciprofloxacin was recommended.

Garamycin was prescribed for a patient with venous ulcer at a dose of 80 mg q12h which will lead to accumulation of drug and can even cause resistance. As per the literature [6] the adjusted dose of Garamycin in patients having moderate renal failure should be the normal dose given at every 36 hrs.

Also, another antibiotic called cefepime was prescribed for prophylaxis of secondary infection with a dose of 1 g given two times daily. In renal impairment the half-life of cefepime will tend to increase fivefold and will lead to accumulation of drug. This results in increased chance of severe ADR like toxic epidermal necrolysis, encephalopathy and seizures. Hence, 500 mg BD or 1 g OD was recommended.

Another cephalosporin which required dose individualization was Cefoperazone whose usual dose is 2g twice daily but in decreased renal function its level in plasma tend to increase and cause severe ADR like Steven-Johnson syndrome, epidermal necrolysis etc. Hence the dose should be adjusted to 1 gm per day to minimize such complications. Cefepime which does not require any adjustment was substituted as a safe and suitable therapeutic alternative.

Fluroquinolones such as levofloxacin, and ciprofloxacin were prescribed for various infections at a dose of 500 mg once daily. The treatment continued for several days during the hospital stay. In situation of impaired renal function the serum concentration of drug will increase rapidly and tend to cause toxicity. It worsens the renal function as well as it affects the liver. Thus it became mandatory to adjust the dose to 1 g repeated three times per week for levofloxacin and 400mg once daily (max) for ciprofloxacin so that the drug concentration will remain in therapeutic range.

Ofloxacin, which is another fluroquinolones require dose individualization as it causes increased risk of tendonitis and tendon rupture if administered in normal adult doses for patients having renal failure. Thus it was recommended to give half the usual dose to minimize toxicity.

Amikacin, an aminoglycoside antibiotic was administered for symptoms of mycobacterial infection with a dose of 500 mg twice daily for a patient who was in end stage renal diseases (ESRD).In such a condition, the dose of amikacin should be adjusted to avoid complications like nephrotoxicity and ototoxicity. The modified dose in this case was 500mg repeated three times a week.

Diuretics

Few cases with comorbidities like SHT, CHF and CRF were treated with potassium sparing diuretics like spironolactone and eplerenone for edema as well to reduce systemic blood pressure. But for a CRF patient these drugs are recommended to be avoided from pharmacotherapy. Continued use of hydrochlorthiazide 12.5 mg once daily in a CRF case with a past medical history of systemic hypertension was recommended to be stoppedas the cumulative effect of thiazide in body will precipitate azotemia which will further impair the renal function.[6]

Antihypertensives

The current study documented few CRF patients receiving nebivolol, a cardio selective beta-blocker, at a dose of 5 mg OD and angiotensin converting enzyme inhibitor, Ramipril 5mg BD. Nebivolol is a nephrotoxic drug which causes reduced renal blood flow which will further enhance the deleterious effect on renal function. The adjusted dose of nebivolol in such cases was 2.5 mg once daily so that nephrotoxic effects can be minimized [14].

ACE inhibitors like Ramipril is also considered nephrotoxic drug and in most SHT cases it was administered as 5mg twice daily dosage. But international indices[6] suggests that maximum tolerated dose of Ramipril in RF patients is 2.5 mg up to a maximum of 5mg per day.

Antidiabetics

Metformin is a drug frequently prescribed in T_2DM at a dose of 500mg once daily. In renal impairment the elimination of metformin and its metabolites diminishes, leading to drug accumulation. This precipitates fatal condition like lactic acidosis and hence the use of metformin in renal failure patients is contraindicated.

Another antidiabetic drug of interest is glipizide which is usually prescribed at a dose of 2.5 mg twice daily. At this dose accumulation is common in renal impaired patients and will end up in hypoglycemic coma which is very severe. Hence glimipride 1 mg/daywas recommended as suitable therapeutic substitute.

Analgesics

Tapentadol 50mg thrice daily was prescribed in a case having CrCl< 30ml/min. The Area under the Curve (AUC) of tapentadol is higher and lead to nephrotoxicity in such cases. So tapentadol use was recommended to be withdrawn in renal failure patients. In renal impairment the elimination of paracetamol is profoundly diminished which will lead to accumulation of N-acetyl-p-benzoquinone imine (NAPQI), a toxic metabolite of paracetamol in renal tissues and it may lead to complete organ damage[6]. So it was advised to increase the dosing interval of paracetamol to minimize the toxic effects.

Antihyperlipidemics

Rosuvastatin 10mg daily was prescribed in a case with hyperlipidemia and severe renal impairment. Over dosage of rosuvastatin due to reduced elimination can cause breakdown of skeletal muscle tissues (rhabdomylosis) and can aggravate the renal failure conditions.

Based on available evidence, rosuvastatin 5mg OD or atorvastatin 10mg/20mg OD which are safer in renal failure was recommended by the pharmacist.

Other drugs

Injection potassium chloride (KCl) prescribed in a case of CRF was recommended to be withdrawn as it can cause hyperkalemia and related cardiac complications like tachyarrhythmia. Hence the use of KCl should be avoided in such conditions.

An important anticoagulant enoxaparin will have increased exposure in the body as the elimination of drug is drastically reduced in renal failure. This can cause fatal hemorrhagic complications and hence it was suggested to titrate the dose in order to optimize the blood thinning and reduce problems [6].

CONCLUSION

The present study observed that the dosing of drugs in renal impairment follows the standard guidelines to a greater extend and are comparable with the excising literature. However the presence of renal dysfunction was not considered in dosing of certain renally excreted drugs like nebivolol, metformin, glipizide, levofloxacin etc. which in-turn can lead to potential risk for adverse drug reactions. This study clearly showed that pharmacist participation in ward rounds, prescription chart review, evaluation of drug dosing based on eGFR or creatinine clearance and immediate concurrent feedback mechanism may cause substantial reduction of inappropriate drug regimens, thereby improving drug safety in patients with renal impairment.

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Table 1: Demographic Data

S.No	*Parameters*	*Value*
1.	N	50
2.	Mean Age (yrs)	58.46±12.75
3.	Male, n (%)	37(74%)
4.	Female (%)	13 (26%)
5.	Mean Body Weight (kg)	70.8 ±14.02
6.	Mean serum creatinine (mg %)	5.48 ± 3.04
7.	Mean creatinine clearance (mg/ml)	15.5 ±10.05

Table 2: Stages of Renal impairment (N=50)

Stages	*No. of Patients*	*Percentage (%)*
Normal (>80ml/min)	0	0
Mild (60 – 79ml/min)	0	0
Moderate (30 – 49ml/min	13	26
Severe (10 – 29ml/min)	17	34
ESRD (<1ml/min)	20	40

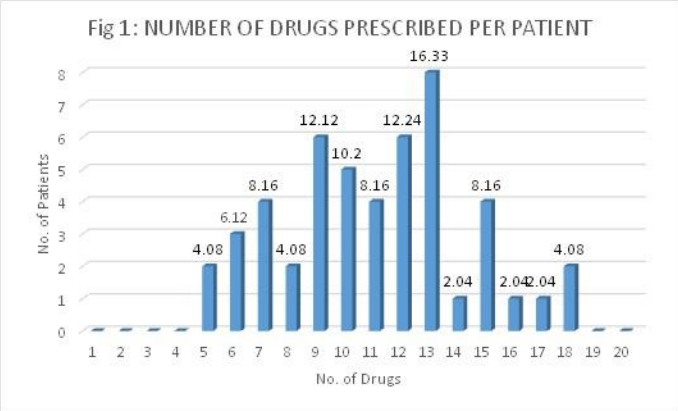

Fig.1: Number of drugs prescribed per patient

Table 3: Prescribing pattern of renally eliminated drugs (N=506)

Sl.No.	*Category*	*Total Drugs*	*Percentage (%)*	*No. of Patients*	*Percentage (%)*
1.	Vitamins & minerals	78	15.41	42	84
2.	Antibiotics	66	13.04	40	80
3.	Antihypertensives	56	11.07	32	64
4.	Antiulcer	47	9.29	41	82
5.	Antiasthmatic	38	7.51	18	36
6.	Analgesics	33	6.52	22	44
7.	Antidiabetics	32	6.32	17	34
8.	Diuretics	31	6.13	23	46
9.	Antiemetic	29	5.73	24	48
10.	Hematopoietic Agents	22	4.25	15	30
11.	Sedatives	11	2.17	8	16
12.	Anticoagulants	11	2.17	11	22
13.	Uricosuric agents	11	2.17	10	20
14.	Anti Hyperlipidemic	9	1.78	9	18
15.	Laxatives	8	1.59	8	16
16.	Anticonvulsants +Antianxiety	6	1.18	6	12
17.	Cortisones	5	0.98	2	4
18.	Antianginal	5	0.98	5	10
19.	Hepatoprotective	4	0.79	3	6
20.	Anti-allergic	3	0.59	5	10
21.	Antidiarrheal	1	0.19	2	4

Table 4: Errors in prescribing renally eliminated drugs and their adjusted dose (N=88)

S.No	*Drugs prescribed*	*No. of patients (%)*				*Prescribed Dose*	*Adjusted Dose*
		30-59ml/min	*15-29ml/min*	*<15ml/min*	*Errors*		
1	Cefoperazone	-	2(2.22)	-	Overdose	1gm BD	1g OD
2	Piperazillin	-	2(2.22)	3(3.33)	Wrong Frequency	4g BD	3g BD
3	Garamaycin	1(1.11)	-	-	Wrong Frequency	80mg q24h	80mg q36h
4	Amoxicillin	-	1(1.11)	-	Overdose	1g BD	500 mg BD/ 1gOD
5	Ofloxacin	-	2(2.22)	2(2.22)	Overdose	200mg OD	100 mg OD
6	Cefepime	-	-	1(1.11)	Overdose	1g BD	500mg BD/1gOD
7	Ciprofloxacin	-	-	1(1.11)	Overdose	500mg OD	400mg od
8	Levofloxacin	-	2(2.22)	1(1.11)	Overdose	500mg OD	1g x 3times/week
9	Amikacin	-	-	1(1.11)	Overdose	500mg BD	500mg x3 times/week
10	Ceftriaxone	-	2(2.22)	9(10)	Overdose	1g OD	22 - 290 mg
11	Tazobactum	-	2(2.22)	3(3.33)	Wrong Frequency	500mg BD	250mg BD
12	Ramipril	-	2(2.22)	1(1.11)	Overdose	5mg BD	2.5mg BD(CHF)
13	Nebivolol	2(2.22)	-	8(8.89)	Overdose	5mg OD	2.5mg OD
14	Spironolactone	1(1.11)	-	4(4.44)	Contraindicated	25mg BD	Avoid
15	Eplerenone	-	1(1.11)	-	Contraindicated	25mg OD	Avoid
16	Hydrochlorthiazide	-	1(1.11)	-	Contraindicated	12.5mg OD	Avoid
17	Allopuranol	-	-	2(2.22)	Wrong Frequency	100mg BD	100mg OD
18	Febuxostat	1(1.11)	-	5(5.56)	Overdose	40mg OD	2.5 - 14mg
19	Metformin	1(1.11)	1(1.11)	1(1.11)	Contraindicated	500mg OD	Avoid
20	Glipizide	-	1(1.11)	1(1.11)	Contraindicated	2.5mg OD	Avoid
21	Tapentalol	-	1(1.11)	-	Contraindicated	50m OD	Avoid
22	Paracetamol	2(2.22)	1(1.11)	3(3.33)	Wrong Frequency	650mg q4h	650mg q8h
23	Rosuvastatin	1(1.11)	2(2.22)	1(1.11)	Overdose	10mg BD	5mg OD (10mg max)
24	Racecadotril	-	-	1(1.11)	Contraindicated	100mg OD	Avoid
25	Tranexamic acid	1(1.11)	-	-	Overdose	500mg BD	250 mg tid
26	Chlordiazepoxide	-	-	1(1.11)	Overdose	10mg BD	5mg bd
27	Hydroxychloroquine	-	1(1.11)	-	Overdose	200mg OD	50 mg OD
28	Potassium Chloride	1(1.11)	-	-	Contraindicated	150mg TDS	Avoid
29	Sildenafil Citrate	1(1.11)	-	-	Overdose	25mg BD	25mg OD
30	Enoxaparin	-	1(1.11)	-	Overdose	40mg BD	40mg od / 20mg bd
31	Levocitrizine	-	1(1.11)	-	Overdose	5mg OD	2.5mg orally twice weekly
32	Levosulpride	-	1(1.11)	-	Contraindicated	25mg OD	Avoid
33	Clobazam	-	1(1.11)	1(1.11)	Overdose	5mg OD	0.21 - 1.21 mg

Table 5: Types of errors identified (N=33)

Sl. No	*Type of error*	*No. of Patients*	*Percentage (%)*
1.	Overdose	20	60.60
2.	Contraindicated	9	27.27
3	Wrong frequency	4	12.12

Table 6: Prescribed drugs with major interactions and contraindications in renal failure (N=73)

Sl.No	*Drugs*	*Interaction*	*Percentage of Interaction*	*Severity*
1	Furosemide + Metoprolol	Increase the risk of hyperkalemia	1.39	Major
2	Metoprolol + Spironolactone	Increase risk of hyperkalemia	1.39	Major
3	Theophylline + Tramadol	Increased risk of seizures	1.39	Major
4	Hydrocortisone + Doxofylline	Decrease the effect of theophylline	1.39	Major
5	Ceftriaxone + Torsemide	Increase risk of kidney failure	2.79	Major
6	Propoxifen + Clobazam	Increase CNS side effets	1.39	Major
7	Metoprolol + Calcium carbonate	Decrease the effects of metoprolol	1.39	Major
8	Metoprolol + Amlodipine	Reduction heart rate, cardiac contractility	1.39	Major
9	Doxepin + Propoxyphene	Increase the effects other medication	1.39	Major
10	Propoxyphene + Hydroxyzine	Increase the effects such as dizziness, confusion, drowsiness	1.39	Major
11	Theophylline + nebivolol	Increase the effect of theophylline	1.39	Major
12	Ceftriaxone + calcium	Precipitation in lungs & kidney	1.39	Major
13	Nebivolol +calcium	Decreases the effects of nebivolol	1.39	Major
14	Chloroquine + Ondansetron	Increased risk of QT interval prolongation	1.39	Major
15	Isoniazid + Rifamipicin	Results in hepatotoxicity	1.39	Major
16	Potassium chloride + Spiranolactone	Results in hyperkalemia	1.39	Major
17	Tramadol + Levofloxacin	Increased risk of seizures	1.39	Major
18	Ciprofloxacin + Sodium bicarbonate	Increased risk of stone formation	1.39	Major
19	Atenolol + Diclofenac	decreased effect of atenolol	1.39	Major
20	Pantoprazole + Glyburide	Increased action of Glyburide	1.39	Major
21	Aspirin + Hydrocortisone	Aspirin effect gets reduced	1.39	Major
22	Salbutamol + Toresemide	Hypokalemia	1.39	Major
23	Albuterol + Carvedilol	Inhibits activity of albuterol	1.39	Major
24	Levofloxacin + Insulin	Increased effect of insulin	1.39	Major
25	Prochlorperazine + Levofloxacin	Increased QT interval	1.39	Major
26	Furosemide + Ketorolac	Decreased diuresis	1.39	Major
27	Furosemide + Metoprolol	Hypotention	1.39	Major
28	Furosemide + Nebivolol	Hypotension	1.39	Major
29	Eplerenone + Spironlactone	Hyperkalemia	1.39	Contraindicated
30	Clopidogrel + Rabeprazole	Inhibits activity of clopidogrel.	1.39	Contraindicated
31	Ceftriaxone + Calcium gluconate	Results in formation crystals in blood stream	2.79	Contraindicated

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