Drug usage pattern of antimicrobials in elderly hypertensive, diabetic in-patients with or without impaired renal function

Prasan R. Bhandari*, Apeksha Bhandary

Department of Pharmacology, SDM College of Medical Sciences and Hospital, Dharwad, Karnataka, India

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*Correspondence to:
Dr. Prasan R. Bhandari,
Email: prasangeeta2012@gmail.com

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ABSTRACT

Background: Hypertension (HTN) and diabetes mellitus (DM) are the primary contributors to renovascular mortality and morbidity including chronic kidney diseases. Additionally, these patients are in frequent need of an antimicrobial agent. Drug utilisation studies (DUS) are prospective tools in the assessment of health care systems. The objective of the present study was to analyse the prescription pattern of anti-microbials in elderly hypertensive diabetic in-patients with or without renal impairment in a tertiary hospital

Methods: The study population comprised of 165 hypertensive diabetic in-patients at Shri Dharmasthala Manjunatheshwara (SDM) Hospital. Questionnaire based evaluation was carried out and prescriptions of patient with HTN and DM at and above the age of 60 years irrespective of gender were included.

Results: Among anti-microbial agents, other β lactam antibacterial were the most commonly prescribed class of drugs (40.85%) which was similar in patients with impaired renal function (21.8%).

Conclusions: There was a significant increase in the number of anti-microbial agents and other drugs in the patients with impaired renal function when compared to patients with normal renal function (p <0.05).

Keywords: Antimicrobial, Drug utilization, Renal impairment

INTRODUCTION

Chronic kidney disease (CKD) is characterized by multiple disorders affecting the morphology and function of kidneys.1 It is estimated on the basis of a decrease in the number of nephrons, which ultimately decreases the glomerular filtration rate (GFR) for a period more than 3months.2 Hypertension and diabetes, recurrent infections along with an inappropriate prescription of drugs are the leading factors resulting in the increasing incidence of CKD.3,4 CKD accounts for 850,000 deaths worldwide as reported by World Health Organization.5

Pharmacokinetics in renal compromised patients is altered and often results in drug accumulation and toxicity.6 Diabetes, hypertension, and renovascular diseases are the common causes of CKD in developing countries, whereas in the tropical countries, infection induced glomerular disease contributes the most to CKD.3,7 Hence, the utilization pattern, marketing and distribution of drugs widely varies with time, geographical distribution, health economics, and sociomedical parameters.8

Due to diverse co-morbid conditions and complications, physicians have to use multiple drugs in the management of CKD, which, on the contrary, results to drug interaction and suboptimal action. CKD patients are more susceptible to infections and are likely to be prescribed with antimicrobial agents. The dosing of all drugs, including antibiotics should be optimized and monitored so as to prevent adverse drug reactions, avoid further renal injury and to facilitate treatment outcomes.9-11

Antimicrobials may well be required in CKD patients for reasons such as urinary or respiratory tract infections. However, since many antibiotics are renally eliminated
and some may be nephrotoxic in nature, careful antibiotic drug and dose selection are necessary. The lack of a clear indication for antibiotic therapy in 82.05% cases is, therefore, a matter of concern.

Drug utilisation studies carries an important role in clinical scenarios as it is the base for generating amendments in the drug dispensing guidelines at local and national levels. The ensuing objective of such study is to support rational drug use. Additionally, as it assists in formulating policies to utilize health resources in the most effective method, it is essentially necessary in a developing economy like India where health care burden is endured by the patients.

The reference standard for drug utilisation is WHO ATC/DDD (Anatomical Therapeutic Chemical/Defined daily dose) methodology.12 Defined daily dose (DDD) is defined by the WHO Collaborating Centre for Drug Statistics and Methodology as the expected average maintenance adult dose per day for its main indication for each drug and route of administration. The DDD thus is an international unit assisting in international or regional comparisons. However, DDD does not fundamentally disclose the recommended or prescribed daily dose (PDD). Nonetheless, a number of studies have described inconsistencies between DDD and PDD for different groups of drugs.13-16 Hence a drug utilization study was conducted to evaluate the drug utilization pattern of antimicrobial medicines during hospital stay and at the time of discharge, cost of antidiabetic drugs and defined daily dose (DDD)/100 bed-days during hospital stay in our setup.

DUS can identify the frequent prescribing errors, their causes, the deviation from the guidelines, and the cost effectiveness. In the present study we intend to:

- Analyse the drug usage pattern of anti-microbials in elderly hypertensive diabetic in-patients in a tertiary hospital.
- Analyse drug usage pattern of anti-microbials in elderly hypertensive, diabetic in-patients with renal impairment in a tertiary hospital.

METHODS

Study design

It was a prospective, observational study carried out at medicine wards in SDM College of Medical Sciences and Hospital, Karnataka. The study protocol was approved by the Institutional ethics committee (IEC). All the patients were explained clearly about the nature and purpose of the study in their own language and consent was taken.

Inclusion criteria

- Patients of either sex at and above 60 years admitted in the medicine wards diagnosed with HTN and DM and were on treatment with anti-diabetics,
- Patients whose renal profile (Serum creatinine) is available after their admission to the hospital.

Exclusion criteria

- Patients less than 60 years of age,
- Patients diagnosed with HTN or DM but not both,
- Patients whose renal profile data was not available,
- Patient/ relative who were not willing to give their consent or were unable to give consent,
- No sufficient data (age, registration number) were available,
- Patients having emergency/life threatening medical/ surgical conditions.

Sample size

A total of 165 hypertensive and diabetic patients clinically diagnosed as per JNC 7 and American Diabetes Association (ADA) at SDM Medicine wards were enrolled.

Participants and data collection

A questionnaire-based study was conducted at the medicine wards. Prescriptions of clinically diagnosed HTN and DM patients at and above the age of 60 years admitted in the medicine wards were included. The questionnaire consisted patient’s demographics like age, gender, marital status, religion and registration number. Patient’s diagnosis was made as per JNC 7 and ADA 2015. Renal function tests were obtained and creatinine clearance (Cr. Cl) calculated using Cockcroft-Gault equation, BP recording and BS levels, (Random blood sugar (RBS), fasting blood sugar (FBS), and glycosylated haemoglobin (HbA1c), if done, then the values were noted.

Statistical analysis

Descriptive statistics was applied. Data was analysed by proportion and percentages and comparison done using chi-square test using Statistical Package for the Social Sciences (SPPS) software version 24.

RESULTS

In the study population majority 88 (53.33%) of the patients had impaired renal function and 77 (46.67%) of patients had normal renal function (Figure 1). A total of 142 antimicrobial agents excluding FDCs were prescribed for 165 patients. Among them ATC class J01D (other β lactam antibacterials) was most commonly used 40.85% (n=58) of which ceftriaxone was used more frequently (35.21%), followed by class J01F (macrolides, lincosamides and streptogramins) (13.38%). Among patients with impaired renal function too ceftriaxone was the commonest drug prescribed (17.6%) (Table 1).
Table 1: Antimicrobial agents prescribed to the study population.

| Class/ATC classification | Generic name | Total | Impaired renal function | Total | Impaired renal function |
|--------------------------|--------------|-------|-------------------------|-------|-------------------------|
|                          |              |       | Yes | % | No | % | Yes | % | No | % |
| ATC                     | Drug name    |       |     |   |     |   |     |   |     |   |
| J01A                    | J01AA02 - Doxycycline | 8 | 5.63 | 6 | 4.2 | 2 | 1.4 |
| J01C                    | J01CA01 - Ampicillin | 1 | 0.70 | 1 | 0.7 | 0 | 0.0 |
| J01D                    | J01DC02 - Cefuroxime | 3 | 2.11 | 2 | 1.4 | 1 | 0.7 |
|                         | J01DD04 - Ceftriaxone | 50 | 35.21 | 25 | 17.6 | 25 | 17.6 |
|                         | J01DE01 - Cefepime | 1 | 0.7 | 1 | 0.7 | 0 | 0.0 |
|                         | J01DH02 - Meropenem | 3 | 2.11 | 2 | 1.4 | 1 | 0.7 |
|                         | J01DI03 - Faropenem | 1 | 0.7 | 1 | 0.7 | 0 | 0.0 |
| J01F                    | J01FA09 - Clarithromycin | 9 | 6.34 | 5 | 3.5 | 4 | 2.8 |
|                         | J01FA10 - Azithromycin | 10 | 7.04 | 5 | 3.5 | 5 | 3.5 |
| J01G                    | J01GB06 - Amikacin | 1 | 0.7 | 0 | 0.0 | 1 | 0.7 |
| J01M                    | J01MA12 - Levofoxacin | 3 | 2.11 | 2 | 1.4 | 1 | 0.7 |
|                         | J01MA14 - Moxifloxacin | 8 | 5.63 | 5 | 3.5 | 3 | 2.1 |
| J01X                    | J01XA02 - Teicoplanin | 6 | 4.23 | 5 | 3.5 | 1 | 0.7 |
|                         | J01XE01 - Nitrofurantoin | 3 | 2.11 | 2 | 1.4 | 1 | 0.7 |
|                         | J01XX08 - Linezolid | 9 | 6.34 | 4 | 2.8 | 5 | 3.5 |
| J02A                    | J02AC01 - Fluconazole | 2 | 1.41 | 0 | 0.0 | 2 | 0.0 |
| P01A                    | P01AB01 - Metronidazole | 6 | 4.23 | 1 | 0.7 | 5 | 3.5 |
|                         | P01AB03 - Ornidazole | 11 | 7.75 | 10 | 7.0 | 1 | 0.7 |
| P01B                    | P01BE03 - Artesunate | 1 | 0.7 | 0 | 0.0 | 1 | 0.7 |
| P02C                    | P02CA03 - Albendazole | 6 | 4.23 | 3 | 2.1 | 3 | 2.1 |
| Total                   | Total | 142 | 100.0 | 80 | 56.3 | 62 | 43.7 |

Figure 1: Impaired renal function in the study participants.

The average PDD/DDD for the most commonly prescribed drugs ceftriaxone and ornidazole was 1 and 1.28 respectively in our study population. PDD/DDD ratio ranged between (0.30-2.25), least being for cefepime (0.26) and maximum for doxycycline (2.25). The range of PDD/DDD for drugs with impaired renal function was (0.28-2.30). For faropenem no DDD is defined when the study was conducted (Table 2).

Among the 142 anti-microbial agents prescribed majority of drugs were BD dosing 95 (66.90%), followed by OD dosing 29 (20.42%). IV route of administration was the most commonly used route prescribed for antimicrobial agents, 113 (79.58%), followed by oral route 29 (20.42%) (Table 3).

A total of 88 antimicrobial FDCs were prescribed for 165 patients. Among them ATC class J01CR (Combination of penicillins inclusive of β lactamase inhibitors) was most commonly used 47.7% (42) of which piperacillin + tazobactam was used more frequently (38.6%), followed by class J01DD (3rd generation cephalosporins) (37.5%). Among patients with impaired renal function too piperacillin + tazobactam was the commonest FDCs prescribed (29.5%) (Table 4).

The average PDD/DDD for the most commonly prescribed FDC drugs piperacillin + tazobactam and cefopazone + tazobactam was 0.63 and 0.85 respectively in our study population. PDD/DDD ratio ranged between (0.37 - 0.71), least being for cefopazone + sulbactam (0.37) and maximum for amoxicillin + clavulanic acid (0.71). The range of PDD/DDD for drugs with impaired renal function was (0.16 - 0.75) (Table 5).

Among the 88 antimicrobial FDCs prescribed majority of drugs were BD dosing 69 (78.41%), followed by TID dosing 16 (18.18%). IV route of administration was the
most commonly prescribed route of administration (94.3%) for antimicrobial FDCs (Table 6).

Table 2: Average PDD/DDD of antimicrobial agents in the study population.

| Antimicrobial Agent | Total PDD/DDD | Impaired Renal Function |
|---------------------|---------------|-------------------------|
|                     |               | Yes | No  |
| Albendazole         | 1.00          | 1.00 | 1.00 |
| Amikacin            | 1.00          | 0   | 1.00 |
| Ampicillin          | 1.00          | 1.00 | 0.00 |
| Artesunate          | 0.43          | 0   | 0.43 |
| Azithromycin        | 1.47          | 1.40 | 1.53 |
| Cefepime            | 0.30          | 0.30 | 0.00 |
| Ceftriaxone         | 1.00          | 1.00 | 1.00 |
| Cefuroxime          | 0.67          | 0.80 | 0.50 |
| Clarithromycin      | 1.67          | 1.80 | 1.50 |
| Doxycycline         | 2.25          | 2.30 | 2.00 |
| Faropenem           | -             | -   | -   |
| Fluconazole         | 0.88          | 0.00 | 0.87 |
| Levofloxacin        | 1.00          | 1.00 | 1.00 |
| Linezolid           | 1.00          | 1.00 | 1.00 |
| Meropenem           | 1.17          | 1.00 | 1.50 |
| Metronidazole       | 0.94          | 1.00 | 0.93 |
| Moxifloxacin        | 1.13          | 1.20 | 1.00 |
| Nitrofurantoin      | 1.33          | 1.50 | 1.00 |
| Ornidazole          | 1.28          | 1.20 | 1.50 |
| Teicoplanin         | 0.58          | 0.60 | 0.50 |

Out of 165 patients, 42.42% (70) of patients C/S tests was done and 57.58% (95) of patients C/S was not done. Out of 70 C/S reports in the study participants, most common (17.14%) organism found was *Escherichia coli*, followed by enterococcus species (8.57%). No growth in the C/S was seen in 41.43% (29) of patients (Figure 2 and 3).

Table 3: Frequency and route of administration of antimicrobial agents in the study population.

| Frequency | n  | %   | Route | n  | %   |
|-----------|----|-----|-------|----|-----|
| OD        | 29 | 20.42 | IV    | 113 | 79.58 |
| BD        | 95 | 66.90 | Oral  | 29  | 20.42 |
| TID       | 10 | 7.04  |       |     |      |
| STAT      | 8  | 5.63  | Total | 142 | 100.00 |

Out of 70 C/S reports in the study participants, a total of 350 antimicrobial agents were found to be resistant.

Maximum, 26 (7.43%) antimicrobial resistance was seen for the drug ciprofloxacin, followed by ampicillin 5.43%.
(19), cefuroxime 5.43% (19), co-trimoxazole 5.43% (19), gentamycin 5.43% (19), ceftriaxone 4.86% (17), nalidixic acid 4.86% (17), amoxicillin 4.57% (16), cefepime 4.57% (16), cefotaxime 4.29% (15), cefuroxime axetil 4.29% (15), amoxicillin + clavulanic acid 3.14% (n=11), clindamycin 2.29% (8), erythromycin 2.00% (7), levofloxacin 2.00% (7), tetracycline 2.00% (7).

Table 4: Antimicrobial FDCs prescribed for the study population.

| Class/ATC classification | Total | Impaired renal function | Generic name | Total | Impaired renal function |
|--------------------------|-------|--------------------------|--------------|-------|-------------------------|
| ATC code                 |       | Yes | No | Yes | No | Drug name | n | % | n | % | n | % | n | % |
| A02BD                    | 1     | 1   | 1  | 0   | 0  | A02BD06-Amoxicillin+Clarithromycin+Esomeprazole | 1 | 1.1 | 1 | 1.0 | 0 | 0.0 |
| J01CR                    | 42    | 47.7 | 30 | 34.1 | 12 | 13.6 | J01CR02-Clarithromycin+Clavulanic Acid | 8 | 9.1 | 4 | 4.5 | 4 | 4.5 |
|                          |       |     |   |     |    | J01CR05-Piperacillin+Tazobactum | 34 | 38.6 | 26 | 29.5 | 8 | 9.1 |
| J01DD                    | 33    | 37.5 | 25 | 28.4 | 8  | 9.1 | J01DDL54-Ceftixalone+Tazobactum | 12 | 13.6 | 11 | 12.5 | 1 | 1.1 |
|                          |       |     |   |     |    | J01DDL62-Cefoperazone+Sulbactum | 4 | 4.5 | 3 | 3.4 | 1 | 1.1 |
|                          |       |     |   |     |    | J01DDL62-Cefoperazone+Tazobactum | 17 | 19.3 | 11 | 12.5 | 6 | 6.8 |
| J01DH                    | 4     | 4.5 | 4  | 4.5 | 0  | 0.0 | J01DHS5-Imipenem+Cilastatin | 4 | 4.5 | 4 | 4.5 | 0 | 0.0 |
| J01R                     | 5     | 5.7 | 2  | 2.3 | 3  | 3.4 | J01R-Cefepime+Tazobactum | 4 | 4.5 | 1 | 1.1 | 3 | 3.4 |
|                          |       |     |   |     |    | J01R-Ornidazole+Cefixime | 1 | 1.1 | 1 | 1.1 | 0 | 0.0 |
| J01RA                    | 2     | 2.3 | 0  | 0.0 | 2  | 2.3 | J01RA09-Ornidazole+Ofloxacin | 2 | 2.3 | 0 | 0.0 | 2 | 2.3 |
| J04AM                    | 1     | 1.1 | 0  | 0.0 | 1  | 1.1 | J04AM06-Isoniazid+Rifampacin+Pyrizinamide+Ethambutol | 1 | 1.1 | 0 | 0.0 | 1 | 1.1 |
| Total                    | 88    | 100 | 62 | 70.5 | 26 | 29.5 | Total | 88 | 100 | 62 | 70.5 | 26 | 29.5 |

Table 5: Average PDD/DDD of antimicrobial FDC in the study population.

| Drug name | Total | Impaired renal function | Total | Impaired renal function |
|-----------|-------|--------------------------|-------|--------------------------|
|           |       | Yes | No | Yes | No | Drug name | Total | Impaired renal function | Total | Impaired renal function | Total | Impaired renal function |
| A02BD06-Amoxicillin+Clarithromycin+Esomeprazole |       |     |   |     |   | Amoxicillin+Clarithromycin+Esomeprazole |       |     |   |     |   | Amoxicillin+Clarithromycin+Esomeprazole |
| J01CR02-Clarithromycin+Clavulanic Acid |       |     |   |     |   | Amoxicillin+Clavulanic Acid | 0.71 | 0.75 | 0.66 | 0.71 | 0.75 | 0.66 |
| J01CR05-Piperacillin+Tazobactum |       |     |   |     |   | Cefepime+Tazobactum |       |     |   |     |   | Cefepime+Tazobactum |
| J01DDL54-Ceftixalone+Tazobactum |       |     |   |     |   | Cefoperazone+Sulbactum | 0.37 | 0.16 | 0.5 | 0.37 | 0.16 | 0.5 |
| J01DDL62-Cefoperazone+Sulbactum |       |     |   |     |   | Ceftriaxone+Tazobactum |       |     |   |     |   | Ceftriaxone+Tazobactum |
| J01DHS5-Imipenem+Cilastatin |       |     |   |     |   | Imipenem+Cilastatin | 0.56 | 0.56 | 0.00 | 0.56 | 0.56 | 0.00 |
| J01R-Cefepime+Tazobactum |       |     |   |     |   | Isoniazid+Rifampacin+Pyrizinamide+Ethambutol |       |     |   |     |   | Isoniazid+Rifampacin+Pyrizinamide+Ethambutol |
| J01R-Ornidazole+Cefixime |       |     |   |     |   | Ornidazole+Cefixime |       |     |   |     |   | Ornidazole+Cefixime |
| J01RA09-Ornidazole+Ofloxacin |       |     |   |     |   | Ornidazole+Ofloxacin |       |     |   |     |   | Ornidazole+Ofloxacin |
| J04AM06-Isoniazid+Rifampacin+Pyrizinamide+Ethambutol |       |     |   |     |   | Piperacillin+Tazobactum | 0.63 | 0.60 | 0.71 | 0.63 | 0.60 | 0.71 |

Table 6: Frequency and route of administration for antimicrobial FDCs in the study population.

| Frequency | n  | %   | Route | N  | %   |
|-----------|----|-----|-------|----|-----|
| OD        | 2  | 2.27| IV    | 83 | 94.3|
| BD        | 69 | 78.41| Oral  | 5  | 5.7 |
| TID       | 16 | 18.18|       |    |     |
| QID       | 1  | 1.14|       |    |     |
| Total     | 88 | 100.0| Total | 88 | 100.0|

DISCUSSION

Among 230 antimicrobial agents prescribed for 165 patients, 88 were FDCs and 142 single drugs. In patients with impaired renal function a total of 142 antimicrobial agents were prescribed. There was a significant difference in the no. of drugs used in the patients with impaired renal function and in patients with normal renal function, (p <0.05). Out of 142 drugs, the most common, 40.85% (n=58) class of antimicrobial agents prescribed were other β lactam antibacterials, followed by macrolides,
linocosamides and streptogramins, 13.38% (n=19), Ceftriaxone was the most frequently 35.21% (n=50) prescribed antimicrobial agent, followed by ornidazole 7.75% (n=11), azithromycin 7.04% (n=10). This was in contrast to a study on patients with DM conducted by Ramachandran G et al, where fluoroquinolones was most commonly prescribed (48%), followed by penicillins and cephalosporins (11%) each.\textsuperscript{17}

In patients with impaired renal function 56.3% (n=80) antimicrobial agents were used with β lactam antibiotics being the most frequently prescribed, 21.8% (n=31), followed by anti-amoebic drugs 8.5% (n=12). Ceftriaxone was the most common drug prescribed in patients with impaired renal function, 17.6% (n=25) followed by ornidazole, 7% (n=10) when compared to patients with normal renal function where ceftriaxone was prescribed, 17.6% (n=25) and ornidazole only once (0.7%).

PDD/DDD ratio ranged between (0.30 - 2.25), least being for cefepine (0.26) and maximum for doxycycline (2.25). The range of PDD/DDD for drugs with impaired renal function was (0.28 - 2.30).

A total of 88 FDCs were prescribed, among which penicillins in combination with β lactamase inhibitors were frequently prescribed, 47.7% (n=42). Out of this piperacillin + tazobactum combination was prescribed in majority, 38.6% (34). Next in line was combination of cephalosporins, 37.5% (n=33), out of this cefoperazone + tazobactum was frequently prescribed (29.5%). Among patients with impaired renal function 62 (70.5%) FDCs were prescribed, which were more in number to that of patients with normal renal function to whom merely 29.5% (n=26) were prescribed. In a study conducted by Santra et al, in patients with CKD azithromycin and levofloxacin were the two drugs most frequently prescribed oral antimicrobial agents used. Cefoperazone, piperacillin + tazobactum, on the other hand, were the most utilized parenteral antibiotics which was similar to present study.\textsuperscript{18}

A total of 230 antimicrobial agents were prescribed among which 88 were FDCs. Other β lactam antibacterials were the most common class of drug prescribed and combination of penicillins with β lactamase inhibitors were the most common FDCs prescribed in patients with or without impaired renal function.

As per the WHO indicators, the average no. of drugs per patient was 9.64±3.123 and with patients with impaired renal function tests was 10.05±3.081, with the least being 4/patient and maximum upto 20/patient. This is at par compared to study by Abraham et al, in elderly where the average no. of drugs is 9.09, is less compared to study by Bajait et al, in patients with CKD where the average is 9.47, and is more when compared to study by Santra et al, in patients with CKD, where the average is 8.1±3.2.\textsuperscript{17,19,20} The practice of polypharmacy is a common finding in similar studies in CKD patients with average number of drugs per prescription varying from 8 to 12.3. In this study only, the prescribed medicines were considered but it is well-known that over the counter use of medicines is common in India. This further increases the chances of drug interactions and adverse reactions.\textsuperscript{21}

Percentage of drugs prescribed by generic names is 6% (n=92) which is much lower to the study conducted by Jhaveri et al, where 48.79% of drugs were prescribed by generic names.\textsuperscript{22}

Percentage of encounters with an antibiotic prescribed was 14.05% and with an injection prescribed was 46.01% and percentage of drugs prescribed from essential drug list was 64.4%.

There was a significant difference in the total number of drugs, antihypertensive drugs, antimicrobial agents and other drugs used in patients with impaired renal function when compared to patients with normal renal function. A mean of 9.64±3.123 drugs per patients were used in present study population and a mean of 10.05±3.081 drugs per patient were used in patients with impaired renal function. Polypharmacy was seen in the present study and is a common finding in majority of studies in India in elderly and in patients with impaired renal function which further increases the risk of drug interactions and adverse drug reactions which are relatively common in elderly and in patients with impaired renal function.

Percentage of drugs prescribed in generic names was minimal when compared to drugs prescribed in brand names, which was in majority in the present study. Generic drug prescription would be advised since majority of the patients are from class IV socioeconomic status and generic drugs prescriptions are cost effective.

Appropriate drug selection for patients with CKD is important to avoid unwanted drug effects and to ensure optimal patient outcomes. Rational drug prescription is difficult in CKD patients due to a higher risk of drug-related problems since they need complex therapeutic regimens requiring frequent monitoring and dosage adjustments. The presence of other comorbidities such as diabetes mellitus, hypertension, coronary artery disease, and infections make the situation more complicated. Inappropriate medication use can increase adverse drug effects as reflected in prolonged hospital stays, increased healthcare utilization and costs.\textsuperscript{23}

The median (IQR) number of drugs per prescription was 10 (9-13) which indicates polypharmacy. Polypharmacy has been defined as the use of 5 or more medications to one patient at a time.\textsuperscript{24} However, in view of the complex nature and coexisting comorbidities of CKD, some researchers suggest the use of more than 9 drugs at a time to be considered polypharmacy.\textsuperscript{24} Inappropriate polypharmacy can lead to significant morbidities and mortality.\textsuperscript{25}

The accumulation and toxicity of many drugs can develop rapidly if dosages are not adjusted in patients with renal
impairment. Kidney disease studies have shown that the cases of chronic kidney disease are growing dramatically over the past 20 years. More than half of the adverse drug effects are due to the inappropriate dosage adjustments. Correctly adjusting the drug dosage in renal dysfunction, contributes to fewer adverse drug effects and decreases the therapeutic costs, hospitalization, length of hospital stays and mortality as well as maintaining therapeutic effectiveness.

This study included only 165 prescriptions for analysis. Additionally, this was only a unicentric study. A large-scale multicentric study would be the future option to conclusively analyse the prescription pattern.

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