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Original article

# Awareness among Patients Regarding Drug Dose Adjustment in Chronic Kidney Disease

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## Abstract

**Background:** Inappropriate medication dosing in patients with chronic kidney disease can cause toxicity or ineffective therapy. Patients are at a high risk of developing related adverse events caused by the altered effect of drugs in conjunction with the use of polypharmacy to treat comorbid conditions. **Aim:** The aim of this work was to highlight the awareness among patients and doctors regarding dose adjustment in chronic kidney disease. **Methods:** This is cross-sectional study was carried out in Benha University hospitals in Internal Medicine, Cardiology, Hepatology, Pulmonology, and Neuropsychiatry Departments on different doctors and patients in the wards using questionnaire. The questionnaire included the following items: Demographic data, Occupational history, Education history, and Personal/family history of kidney disease. **Results:** Regarding questions asked to patients, 55% knew that patients with CKD need dose adjustment, 14% knew drugs need to be adjusted and 9% knew percentage of drugs need to be adjusted. **Conclusions:** Regarding questions asked to doctors, 97% knew that patients with CKD need dose adjustment, 91% knew drugs need to be adjusted, 84% knew Percentage of drugs adjusted and 66% knew level of GFR a given medication needs to be adjusted. Patients across all levels of training demonstrated poor awareness and knowledge of individualizing therapy based on patient's renal function. Poor knowledge of renal dosing rules and lack of medication information have been identified as major causes of prescribing errors.

**Keywords:** Awareness, Drug Dose Adjustment, Chronic Kidney Disease.

**Introduction:**

Chronic kidney disease (CKD) is an important health problem with a rising incidence and prevalence worldwide. Over the past two decades, there has been a 10–20% increase in incidence and prevalence of CKD stages 3–5. This prevalence is even higher in patients with pre-diabetes (18%), diabetes (40–42%) and the elderly (23–58%). The elderly is a growing population with demographic models projecting their number to increase to about 1 in 5 people by the year 2030 [(1)].

CKD is a progressive decline in GFR such that kidney function is reasonably stable over weeks or months. Drug absorption from the gastrointestinal tract may be highly variable in patients with CKD. Although it is commonly thought that absorption decreases in oedematous states because of gut wall oedema, animal and human studies indicate that drug absorption may actually increase because of impairment of the gut wall barrier function or a decrease in function and/or expression of efflux transporters, such as P-glycoprotein [(2)].

The decrease in GFR with CKD decreases kidney drug clearance. A practical approach to adjusting drug doses in CKD is to assume that kidney drug clearance will decrease in proportion to GFR, and that non-kidney clearance is unchanged. However, this otherwise convenient approach is limited by changes to non-kidney clearance that occur with kidney disease and are difficult to quantify at the individual level. It also ignores the role of intact kidney tubules in the handling of many drugs and that tubular elimination likely increases relative to glomerular clearance in some types of kidney disease [(3)].

Many medications require dose adjustment in patients with CKD. Incorrect drug dosing was reported in 23.4% of patients, the majority of whom had renal impairment [(4)].

Drug dosing errors can result in adverse effects, poor patient outcomes, and contribute to excess financial expenditures. Adverse drug events are one of the top 7 leading causes of death in US and Canada [(5)].

Progression of CKD to end-stage renal failure (ESRF) has tremendous human and economic implications. Mortality is as much as 17-fold higher in patients with ESRF compared to age- and gender-matched healthy individuals, and the cost of dialysis or transplantation is frequently unaffordable to many in the absence of governmental programs [(6)]. Therefore, it is important to determine if doctors are obtaining the knowledge necessary to correctly dose

medications in a CKD population. The aim of this work was to highlight the awareness among patients and doctors regarding dose adjustment in chronic kidney disease.

**Methods:**

This cross-sectional study was carried out in Benha University Hospitals in Internal Medicine Department, Cardiology, Hepatology, Pulmonology, and Neuropsychiatry Departments on 100 patients in the period from January 2022 till June 2022. This study included different patients in ward in Internal Medicine Department.

The study was done after being approved from the institutional ethical committee, Benha University and informed consent was obtained from all participants included.

**Inclusion Criteria**

Patients admitted to medical wards with diagnosis of CKD during the study period, age 18 years and above, receiving at least one pharmacological agent, and who had at least one estimated GFR value of $\leq 60$ mL/min/1.73 $m^2$ were included in this study.

**Exclusion Criteria**

Patients who were critically ill, with severe psychiatric illness, and with incomplete medicine record were excluded from the study.

All participants answered a self-build questionnaire including the following items: 1- Demographic data including (age, sex Urban or rural type of residence), 2- Occupational history, 3-Education history, 4- Personal/family history of kidney disease: personal history and/or history of kidney problems among spouse or children, and presence or absence of kidney problems in any first-degree relatives).

5- The following questions were included (for patients and doctors): Do patients with CKD need dose adjustment? What drugs need to be adjusted?

A list of 26 commonly used medications was compiled representing 7 different medication classes: allergy (diphenhydramine, loratadine, montelukast), analgesic (acetaminophen, ibuprofen, meperedine, tramadol), cardiovascular (amlodipine, atenolol, carvedilol, digoxin, enalapril, hydralazine, simvastatin), endocrine (glipizide, pioglitazone, sitagliptin), gastrointestinal (famotidine, pantoprazole), neuropsychotropic (alprazolam, gabapentin, haloperidol, levetiracetam, paroxetine), and rheumatologic (allopurinol, colchicine).

For patients who were answering the questionnaire, we offered the following possible responses to each medication: a)

Does not need dose adjustment, b) Needs dose adjustment, c) I don't know.

For doctor who were answering the questionnaire, we offered the following possible responses to each medication: a) Does not need dose adjustment, b) Needs dose adjustment at glomerular filtration rate (GFR) < 90 ml/min, c) Needs dose adjustment at glomerular filtration rate (GFR) < 60 ml/min, d) Needs dose adjustment at glomerular filtration rate (GFR) < 30 ml/min, e) I don't know.

Percentage of drugs adjusted.

Outcome variables: One outcome was to assess the awareness among patients whether a given medication needed dose adjustment in patients with impaired renal function ('medication dose needs adjustment' awareness). The other outcome was to assess the knowledge among doctors whether they knew at what level of GFR a given medication needs to be adjusted ('medication dose adjustment at appropriate GFR level' knowledge) according to published medication dosing guidelines in CKD. A score of 'one' was assigned for every correct response to a medication. A total score was calculated for each medication class and also for all medications ('overall medication score'). Then Factors affecting awareness of patients were assessed.

**Statistical analysis**

Statistical analysis was done by SPSS v25 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and were compared. Qualitative variables were presented as frequency and percentage (%).

**Research ethics committee: MS.7-9-2021**

**Results:**

Mean age was 51.28 years with SD of 14.11, 55%, were males and 45%, females. Urbans were 62%, and 38%, residence in rural area. Table 1

Regarding occupation 23%,11%,8%,14%,3%,17% and 24% worked as Craftsman, Engineer, Housekeeper, Medical field, Professor, programmer and Teacher respectively. Table 2

Regarding education of included subjects 5%,9%,7%,7%,3%,4% and 65% education levels were Illiterate, Industrial Secondary school, Master degree, Ph.D, Secondary school and University respectively. Table 3

Regarding kidney diseases of included subjects 17% had pervious personal history of kidney disease, 22% had family history and 12% had current kidney disease. Table 4

Regarding questions asked to patients 55% knew that patients with CKD need dose adjustment, 14% knew drugs need to be adjusted and 9% knew Percentage of drugs adjusted. Table 5

Regarding questions asked to doctors, 97% knew that patients with CKD need dose adjustment, 91% knew drugs need to be adjusted, 84% knew Percentage of drugs adjusted and 66% knew level of GFR a given medication needs to be adjusted. Table 6

**Table (1):** Patients basal Characteristics

| **Parameter** | Number | Percentage |
|---|---|---|
| **Age (Years)** | | |
| **Mean ± SD** | 51.28 ± 14.11 | |
| **Sex** | | |
| **Male** | 55 | 55%, |
| **Female** | 45 | 45%, |
| **Residence** | | |
| **Urban** | 62 | 62%, |
| **Rural** | 38 | 38%, |

**Table (2):** Occupation history of included subjects.

| **Occupation** | Number | Percentage |
|---|---|---|
| **Craftsman** | 23 | 23%, |
| **Engineer** | 11 | 11%, |
| **Housekeeper** | 8 | 8%, |
| **Medical field** | 14 | 14%, |
| **Professor** | 3 | 3%, |
| **programmer** | 17 | 17%, |
| **Teacher** | 24 | 24%, |

**Table (3):** Education history of included subjects.

| **Education** | Number | Percentage |
|---|---|---|
| **Elementary** | 5 | 5%, |
| **Illiterate** | 9 | 9%, |
| **Industrial Secondary school** | 7 | 7%, |
| **Master degree** | 7 | 7%, |
| **Ph.D** | 3 | 3%, |
| **Secondary school** | 4 | 4%, |
| **University** | 65 | 65%, |

**Table (4):** kidney diseases of included subjects.

| | Number | Percentage |
|---|---|---|
| **Personal history** | 17 | 17%, |
| **Family history** | 22 | 22%, |
| **Current Kidney disease** | 12 | 12%, |

**Table (5):** Patients awareness regarding drug dose adjustment in chronic kidney disease

| Questions | Number | Percentage |
|---|---|---|
| **Does patients with CKD need dose adjustment?** | 55 | 55%, |
| **What drugs need to be adjusted?** | 14 | 14%, |
| **Percentage of drugs adjusted?** | 9 | 9%, |

**Table (6):** Doctor awareness regarding drug dose adjustment in chronic kidney disease.

| Questions | Number | Percentage |
|---|---|---|
| **Does patients with CKD need dose adjustment?** | 97 | 97%, |
| **What drugs need to be adjusted?** | 91 | 91%, |
| **Percentage of drugs adjusted?** | 84 | 84%, |
| **What level of GFR a given medication needs to be adjusted?** | 66 | 66%, |

## Discussion

Kidney damage or decreased renal function for three months or more is clinically considered as CKD. In patients with CKD, the GFR decreases, and/or there are urinary or structural problems in the renal system. It is a progressive condition characterized by a decrease in kidney function of lower than 60 mL/min/1.7m [(7)].

In the present study, the mean age was 51.28 years with SD of 14.11, 55%, were males and 45%, females. Urbans were 62%, and 38%, residence in rural area.

Similar to our results, another study [(8)] aimed to study the level of awareness regarding chronic kidney disease (CKD), its medications, and laboratory investigations among nephrology and urology patients of Quetta. Among the respondents, mean age (±SD) was 30.16 ± 11.62 years, with the majority of respondents being males 74.1% (n = 347).

Previous study in Pakistan reported that 56.5% of (n = 255 CKD) patients were males, and 43.5% were females, indicating a significant proportion of male respondents [(9)]. The global burden of illness study reveals significant gender disparities in the prevalence of CKD across 195 nations. However, the nature of these discrepancies is complex and must be evaluated cautiously, considering all conceivable local and general conditions.

This was in agreement with another study [(10)] which showed that older age was associated with less awareness overall, and black race was associated with more awareness, but the associations were not statistically significant. The increase in

awareness over time can be seen in both the younger and older and white and black subgroups. Similarly, awareness increased in males and females from 1999-2002, but males remained more likely to be aware in all three survey years [10].

Regarding occupation 23%,11%,8%,14%,3%,17% and 24% worked as Craftsman, Engineer, Housekeeper, Medical field, Professor, programmer and Teacher respectively.

This was in agreement with another study [11] which showed that among all variables studied, the following occupations were associated with the most increased risks for CKD: Healthcare Support Occupations, Protective Service Occupations, Food Preparation and Serving Related Occupations, Building and Grounds Cleaning and Maintenance Occupations, Personal Care and Service Occupations, Sales and Related Occupations, Office and Administrative Support Occupations, Farming, Fishing, and Forestry Occupations, Construction and Extraction Occupations, Installation, Maintenance, and Repair Occupations, Production Occupations, and Transportation and Material Moving Occupations.

Regarding education of included subjects 5%,9%,7%,7%,3%,4% and 65% education levels were Illiterate, Industrial Secondary school, Master degree, PhD, Secondary school and University respectively.

Similar to our results, another study [8] showed that the majority of them were graduates 29.7% (n = 139).

Regarding kidney diseases of included subjects 17% had pervious personal history of kidney disease, 22% had family history and 12% had current kidney disease.

Similar to our results, another study [8] showed among the participants, almost three-quarters 73.9% (n = 346) were suffering from CKD for a duration of 1 to 3 years. Respondents included smokers (43.1%, n = 147) and 56.9% (n = 194) who exercised at least 30 min per day. The majority of participants 75.6% (n = 354) were at the first stage of CKD (i.e., having a glomerular filtration rate (GFR) of 90 mL/min/1.73 m2 or higher). In addition to CKD, many respondents had other co-morbidities as well, including hypertension (21%, n = 129), other cardiovascular diseases (including abnormal heart rhythms or arrhythmias, aortic diseases, congenital heart diseases, coronary artery disease, deep vein thrombosis and pulmonary embolism, history of a heart attack, and cardiomyopathy) (10.4%, n = 64), and diabetes (8.8%, n = 54).

Another study [5] showed that comorbidities were present in most of the patients (77.92%), and among them hypertension (148 [64%]), diabetes mellitus (57 [24.67%]), and obstructive nephropathy (36 [15.58%]) were on the top of the list

Regarding questions asked to patients 55% knew that patients with CKD need dose adjustment, 14% knew drugs need to be adjusted and 9% knew Percentage of drugs adjusted.

In a study done by a group of researchers [8], as a principal part of this study, awareness of participants regarding their disease condition was assessed, with the responses of the participants presented in their study. Participants were asked if they know how to control their blood pressure, with the majority of the respondents (60.7%, n = 284) having a positive response, while 39.4% (n = 184) responded either negatively or indicating that they did not know about it. Two- thirds of the respondents (65.4%, n = 306) were aware that a person can lead a normal life with one kidney. More than half of the participants (50.3%, n = 235) were unaware of symptoms that develop due to worsening of disease, while (56.2%, n = 263) responded with either "No" or "Don't know" about what aggravates their kidney function. Almost half of the affected individuals (47.4%, n = 222) have no understanding about the long-term prognosis of the disease.

Moreover, a study [8] showed that majority of the respondents 50.5% (n = 248) responded with "No" and/or "Don't know" about knowing about the brand names and usage of their medications, while 55.5% (n = 260) responded with "No" and/or "Don't know" about knowing the roles of their taken medicines. A total of 62.4% (n = 292) were unaware of the medicines that may impair their kidney function. More than half of the respondents, 57.5% (n = 269), responded with either "No" or "Don't know" in relation to knowing about herbal medicines that could be effective in CKD. Further, 51.9% (n = 243) were aware about unhealthy diets, while 54.1% (n = 253) responded with "Yes" on the item about diets containing high-quality protein, and 55.1% (n = 258) were aware about the foods they should avoid. Another 59.2% (n = 277) were aware about the appropriate daily salt usage for their condition. The majority of the respondents, 49.8% (n = 233), were unaware about laboratory examinations, which they should regularly check, while 59.6% (n = 279) responded with "No" or "Don't know" on the item about understanding of test reports; i.e., the other participants claimed to

have the understanding to interpret their laboratory tests.

Also, the previous study [8] showed that 57.9% (n = 271) were aware of the importance of exercise for fitness, and more than half of participants (51.1%, n = 239) were aware of the evaluation of curative effects of disease, which means they were aware of signs and symptoms that meant the improvement of their health; 62.8% (n = 294) of patients were aware of how to contact a physician in case of query regarding the condition of the disease.

The previous study [8] study highlighted that the awareness of patients regarding CKD is very low in some areas, and the majority of participants were unaware about the progression of the disease and the acts that may aggravate their kidney functions further. In addition, they were not aware of the symptoms that may appear due to worsening of the disease and when to seek help from HCPs.

The majority of graduate respondents in a study reported a good understanding about controlling their blood pressure when elevated, while respondents who had no formal education or had primary education were not aware of how to do so. Education showed a significant association with knowledge on controlling blood pressure [8].

In another study, individuals who displayed a greater number of markers of renal dysfunction had higher odds of being aware of their kidney disease than individuals with kidney dysfunction who did not exhibit clinical markers [12]. Individuals with two to four clinical markers of CKD demonstrated 90% greater odds of CKD awareness compared with those with zero to one marker. Participants who displayed at least five markers of CKD demonstrated non-statistically significant greater odds of awareness relative to participants with zero to one clinical markers of CKD. There was a graded association between each additionally manifested clinical marker and awareness of CKD; this remained significant after adjustment for demographic and socioeconomic factors and diabetes. Adjusting for eGFR mitigated the association.

Despite the high prevalence of CKD and the massive health-care costs incurred by this population, disease awareness remains profoundly low. Worldwide, only 6% of the general population and 10% of the high-risk population are aware of their CKD statuses. CKD awareness ranges from 3.5 to 9.7% in Taiwan, which has the highest ESRD incidence [13].

In China, there is about 8% of CKD awareness in both rural and metropolitan areas, and the awareness increases among the high-risk populations: 12.1% in diabetes, 14.9% in HTN and 26.5% in those with both diabetes and HTN; yet only 2.1% awareness among those without albuminuria, 8.1% in those with microalbuminuria and 14.5% in macroalbuminuria [14; 15].

In the United States**,** NHANES 1999–2000 survey data showed that 8.2% of participants with stage 3 CKD self-reported a history of renal disease [16].

Regarding questions asked to doctors, 97% knew that patients with CKD need dose adjustment, 91% knew drugs need to be adjusted, 84% knew Percentage of drugs adjusted and 66% knew level of GFR a given medication needs to be adjusted.

In a study, the aim was to investigate the frequency of inappropriate dosing according to the degree of renal impairment of the patients at hospital discharge [17]. Physicians may not review the result of the renal function test because of the overwhelming of the other clinical information. Furthermore, it is obvious that CrCl should be calculated and documented for all of the patients with impaired renal function for the benefit of dosage adjustment. The calculation of CrCl with the Cocroft and Gault formula taking into account patient's weight, age and SCr provides an accurate assessment of the renal function.

The awareness of CKD among primary care physicians is equally low. This is in concordance with another study [18] showed that only 6% and 30% of the individuals who have stage 3 and stage 4 CKD, respectively, were seen by nephrologists.

## Conclusions:

Patients across all levels of training demonstrated poor awareness and knowledge of individualizing therapy based on patient's renal function. Poor knowledge of renal dosing rules and lack of medication information have been identified as major causes of prescribing errors. Even with the use of electronic drug prescribing systems, these systems do not often provide guidance on the need for dose modification. With the shortage of nephrologists and the growing CKD population, it is essential that patients receive more nephrology clinical exposure and formal didactic educational training during residency to better manage the complex treatment regimens and minimize morbidity due to medication dosing errors.

## References:

1. **Surana S, Kumar N, Vasudeva A, Shaikh G, Jhaveri KD, Shah H, Mali et al.** Awareness and knowledge among internal medicine house-staff

for dose adjustment of commonly used medications in patients with CKD. BMC Nephrol. 2017;18(1):26.

2. **Nolin TD**. A Synopsis of Clinical Pharmacokinetic Alterations in Advanced CKD. Semin Dial. 2015;28(4):325-9.
3. **Roberts DM, Sevastos J, Carland JE, Stocker SL, Lea-Henry TN**. Clinical Pharmacokinetics in Kidney Disease: Application to Rational Design of Dosing Regimens. Clin J Am Soc Nephrol. 2018;13(8):1254-63.
4. **Schuler J, Dückelmann C, Beindl W, Prinz E, Michalski T, Pichler M**. Polypharmacy and inappropriate prescribing in elderly internal-medicine patients in Austria. Wien Klin Wochenschr. 2008;120(23-24):733-41.
5. **Hassan Y, Al-Ramahi R, Abd Aziz N, Ghazali R**. Drug use and dosing in chronic kidney disease. Ann Acad Med Singap. 2009;38(12):1095-103.
6. **Farag A, Garg AX, Li L, Jain AK**. Dosing errors in prescribed antibiotics for older persons with CKD: a retrospective time series analysis. Am J Kidney Dis. 2014;63(3):422-8.
7. **Lameire NH, Levin A, Kellum JA, Cheung M, Jadoul M, Winkelmayer WC, et al.** Harmonizing acute and chronic kidney disease definition and classification: report of a Kidney Disease: Improving Global Outcomes (KDIGO) Consensus Conference. Kidney Int. 2021;100(3):516-26.
8. **Ahmed J, Azhar S, Ul Haq N, Hussain S, Stájer A, Urbán E, et al.** Awareness of Chronic Kidney Disease, Medication, and Laboratory Investigation among Nephrology and Urology Patients of Quetta, Pakistan. Int J Environ Res Public Health. 2022;19(9).
9. **Chand S, Khan GR**. Evaluation of Health Related Quality of Life in Patients with Chronic Kidney Disease. Asian Journal of Allied Health Sciences (AJAHS). 2021:10-8.
10. **Plantinga LC, Boulware LE, Coresh J, Stevens LA, Miller ER, 3rd, Saran R, et al.** Patient awareness of chronic kidney disease: trends and predictors. Arch Intern Med. 2008;168(20):2268-75.
11. **Rubinstein S, Wang C, Qu W**. Occupational risk and chronic kidney disease: a population-based study in the United States adult population. International journal of nephrology and renovascular disease. 2013;6:53.
12. **Tuot DS, Plantinga LC, Hsu CY, Jordan R, Burrows NR, Hedgeman E, et al.** Chronic kidney disease awareness among individuals with clinical markers of kidney dysfunction. Clin J Am Soc Nephrol. 2011;6(8):1838-44.
13. **Wen CP, Cheng TY, Tsai MK, Chang YC, Chan HT, Tsai SP, et al.** All-cause mortality attributable to chronic kidney disease: a prospective cohort study based on 462 293 adults in Taiwan. Lancet. 2008;371(9631):2173-82.
14. **Liu Q, Li Z, Wang H, Chen X, Dong X, Mao H, et al.** High Prevalence and Associated Risk Factors for Impaired Renal Function and Urinary Abnormalities in a Rural Adult Population from Southern China. PLOS ONE. 2012;7(10):e47100.
15. **Chen N, Wang W, Huang Y, Shen P, Pei D, Yu H, et al.** Community-based study on CKD subjects and the associated risk factors. Nephrology Dialysis Transplantation. 2009;24(7):2117-23.
16. **Coresh J, Byrd-Holt D, Astor BC, Briggs JP, Eggers PW, Lacher DA, et al.** Chronic kidney disease awareness, prevalence, and trends among

U.S. adults, 1999 to 2000. J Am Soc Nephrol. 2005;16(1):180-8.

17. **Sah SK, Wanakamanee U, Lerkiatbundit S, Regmi BM**. Drug dosage adjustment of patients with impaired renal function at hospital discharge in a teaching hospital. J Nepal Health Res Counc. 2014;12(26):54-8.
18. **Plantinga LC, Tuot DS, Powe NR**. Awareness of chronic kidney disease among patients and providers. Adv Chronic Kidney Dis. 2010;17(3):225-36.

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