PILL BURDEN, DRUG CLASS DISTRIBUTION AND FINANCIAL BURDEN FOR BUYING MEDICINES IN DIFFERENT MODALITIES OF CHRONIC KIDNEY DISEASE PATIENTS: CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: The objective of the study was to assess the pill burden (PB), drug class distribution and financial burden for buying medicines in different treatment modalities of chronic kidney disease (CKD) patients.

Methods: A prospective, cross-sectional study was performed in 244 CKD patients and they were divided into 4 groups as follows: pre-dialysis patients (stages 1-5) as group 1, hemodialysis (HD) patients as group 2, peritoneal dialysis (PD) patients as group 3 and renal transplant recipient (RTR) patients as group 4. Data was collected in pre-designed form through direct patient interaction.

Results: Out of 244 CKD patients, PB considering the total number of pills/d in different modalities is 12±5 in pre-dialysis, 10±3 in HD, 13±5 in PD, 14±7 in RTR and for the number of drug classes/d in different modalities is 7±3 in pre-dialysis, 7±2 in HD, 8±3 in PD and 9±3 in RTR. On average mean PB in a number of pills/d is 12±5 and number of drug classes/d is 8±3. Among all the patients, the RTR individuals are having high medicinal expenditure in comparison to the other modalities.

Conclusion: PB for the number of pills/d is highest in RTR and almost similar in different modalities. Great improvement in reducing the PB as well as financial burden directly or indirectly improve the patient compliance as well as the quality of life.

Keywords: Chronic kidney disease, Pill burden, Drug class distribution, Financial burden, Predialysis, Hemodialysis, Peritoneal dialysis, Renal transplant recipient

INTRODUCTION

Chronic kidney disease (CKD) remains a major global public health problem with increasing prevalence, incidence and tremendous cost with poor outcome [1]. In India, the prevalence rate of CKD was estimated to be 12.5% [2]. As per global burden of disease study, CKD is estimated to be 12th among all causes of death and men are more prominently affected. In western countries, hypertension (HTN) and diabetes mellitus (DM) was found to be a 2/3rd cause of CKD [3]. Likely in India, DM and HTN currently accounted 40-60% cause of CKD [4]. CKD patients are more prone to high pill burden (PB) because of multiple co-morbidities and indirectly reducing the adherence to therapy.

PB refers to taking more number of pills (tablets or capsules and other conventional dosage forms) that a patient takes on a frequent basis. Therefore, high PB increases the chances of hospitalization, medication errors and elevated costs not only for pharmaceuticals as well as treatment for adverse events [5]. Several studies have reported that dialysis patients are expected to have a high PB due to severe chronic illness combined with multiple co-morbidities. It has been reported that average dialysis patients take 10 to 12 different types of medications [6, 7]. In chronic conditions, complex medication regimens with high PB lead to non-adherence [8-11]. CKD patients are prone to a greater chance of drug-related problems not only by the pharmacokinetic variations in renal excreted drugs but also by the use of more number of medications to manage the complications and co-morbidities in CKD.

In middle and low-income countries, the financial burden is the main concern for the patients who require treatment for dialysis or kidney transplantation. In 2009, the mumbai kidney foundation (MKF) reports gave a perception in end-stage renal kidney disease (ESRD) cost management stating that each hemodialysis (HD) session in Indian government and corporate hospitals setup would range in between around INR Rs. 150 to Rs. 2000. Annual expenditure for dialysis in India and United States (US) would cost around Rs. 140000 ($3000) and $60,000 respectively. Compared to other countries, even though there is less expenditure for dialysis in India, most of the population (90%) cannot afford it due to economic issues. Whereas kidney transplantation cost ranges from Rs. 50,000 in government hospitals and Rs. 300,000 in some private hospitals and monthly maintenance for post-transplant drugs would cost around Rs. 10,000 ($1200) [12]. Therefore, it is difficult to afford for many people. In CKD, direct healthcare expenditure is greater in patients with anemia than in those without [13] and quality of life issues (ex. fatigue, reduced productivity) are common [14,15]. Recently in many Indian hospitals, so many schemes are being implemented. In the present scenario, in many of the states in developing countries, government and non-government organizations have come forward to help the patients in providing subsidized or free dialysis. However, the financial burden for the medicines is variable in CKD patients. Keeping this situation in view, we have undertaken this study to know the drug class distribution, PB and financial burden for buying medicines in CKD patients among different treatment modalities.

MATERIALS AND METHODS

This was a prospective, cross-sectional study performed in the department of nephrology at Sri Venkateswara Institute of Medical Sciences (SVIMS), a tertiary care teaching hospital, Tirupati for a period of six months from April 2017 to September 2017, which was approved by the institutional ethics committee clearance (622/IEC/2017). A total of 244 patients diagnosed with CKD at all stages were included. Among
244 CKD patients, based on the modality of treatment, 107 patients were under stage 1-5 (pre-dialysis), 58 were in HD, 52 were in peritoneal dialysis (PD) and 27 were in renal transplant recipient (RTR) as per the national kidney foundation/kidney disease outcomes quality initiative (NKF/KDOQI) guidelines [16]. Pregnant women, children below 18 y, psychotic patients and unwilling participants were excluded. Patients information was collected by using a well-designed data collection form which was kept confidential. Patient’s information was collected after explaining the study and receiving their consent by using informed consent form. Topical, inhaled, injectable medications were not included in PB.

Study procedure

Patients were divided into 4 groups as follows: pre-dialysis CKD patients (stages 1-5) as group 1, CKD patients on HD as group 2, CKD patients on PD as group 3 and RTR patients as group 4. The suitable data collection form was used to collect all the necessary information to evaluate PB and financial costs for buying medicines.

### Table 1: Demographic data of study patients

| Demographic data               | Males (n) | Females (n) |
|--------------------------------|-----------|-------------|
| **Age in years(y)**           |           |             |
| 18-59                          | 96        | 54          |
| ≥60                            | 66        | 28          |
| Dependents                     | 51        | 49          |
| Independents                   | 111       | 33          |
| **Occupational details:**      |           |             |
| Agricultural                   | 37        | 10          |
| Government                     | 58        | 31          |
| Private                        | 69        | 39          |

Based on etiology of CKD, the total patients were divided into two subgroups, i.e., diabetic CKDs and non-diabetic CKDs which include HTN, chronic glomerulonephritis (CGN), chronic interstitial nephritis (CIN) and autosomal dominant polycystic kidney disease (ADPKD) [table 2]. While comparing occupational status and etiological factors of CKD we found that diabetic CKD patients were more in employment group and non-diabetic CKD (HTN and CGN) patients were more in the agricultural group.

### Table 2: Etiology of CKD patients of the present study

| Etiology          | No. of patients (n) | Percentage (%) |
|-------------------|---------------------|----------------|
| DM                | 103                 | 42             |
| HTN and CGN       | 117                 | 48             |
| CIN               | 19                  | 8              |
| ADPKD             | 5                   | 2              |

DM-diabetes mellitus, HTN-hypertension, CGN-glomerulonephritis, CIN-chronic interstitial nephritis, ADPKD-autosomal dominant polycystic kidney disease

One-way ANOVA followed by post hoc bonferroni analysis was performed to assess the drug classes and the number of pills/d in different modalities and unpaired t-test was performed to assess PB in different modalities between the age group 18-59 y and ≥60 y [table 3]. When compared with other modalities, mean PB for drug classes/d was found to be highest (14±7) and mean PB for a total number of pills was also found to be highest (9±3) in RTR patients [table 3]. The results showed that there was no significance between mean pills/d among different modalities between the age group 18-59 y and ≥60 y except in PD patients which showed significance (p=0.002*) and for drug classes/d also showed no significance between age groups except in HD which showed significance (p= 0.013*).

### Table 3: Mean pill burden for number of pills and drug classes per day across different modalities

| Modalities | Age | N | Drug classes/d | p value | p value vs pre-dialysis | Total pills/d | p value | p value vs pre-dialysis |
|------------|-----|---|----------------|---------|-------------------------|---------------|---------|-------------------------|
| Pre-dialysis | 18-59 | 48 | 7±3 | 1.000† | 12±5 | 0.252† | 13±5 | 0.426† |
|            | ≥60  | 59 | 7±2 | 1.000† | 12±4 | 0.252† | 13±5 | 0.426† |
|            | mean | 54±5 | 7±3 | 1.000† | 12±5 | 0.252† | 13±5 | 0.426† |
| HD         | 18-59 | 39 | 7±1 | 0.160† | 11±2 | 0.426† | 12±5 | 0.252† |
|            | ≥60  | 19 | 8±2 | 0.160† | 10±3 | 0.426† | 11±2 | 0.426† |
|            | mean | 29±10 | 7±2 | 0.160† | 10±3 | 0.426† | 11±2 | 0.426† |
| PD         | 18-59 | 36 | 8±3 | 0.934† | 14±5 | 0.939† | 15±6 | 0.939† |
|            | ≥60  | 16 | 7±2 | 0.934† | 10±1 | 0.939† | 14±5 | 0.939† |
|            | mean | 26±10 | 8±3 | 0.934† | 10±1 | 0.939† | 14±5 | 0.939† |
| RTR        | 18-59(M) | 20 | 9±2 | 0.102† | 13±5 | 0.002* | 14±5 | 0.228† |
|            | 18-59(F) | 07 | 9±4 | 0.102† | 13±5 | 0.002* | 14±5 | 0.228† |
|            | ≥60  | 0  | 9±3 | 0.102† | 14±7 | 0.517† | 13±5 | 0.228† |

Data are given as number (n) of patients, values expressed in mean±standard deviation. Significant at *p<0.05 probability level, †NS-not significant at the 0.05 probability level, p-value by using one-way ANOVA between age groups and p-value vs pre-dialysis using post hoc bonferroni analysis between different modalities. Abbreviations: HD-hemodialysis, PD-peritoneal dialysis, RTR-renal transplant recipient.
Across different modalities, the PB for different classes of medications was shown in fig. 1. The unpaired t-test was used to find the significant difference between different drug classes of medications and mean pills/d in HD and PD [table 4]. It was observed that there was a statistically significant between different drug classes of medications and mean pills/d in HD and PD (*p<0.05*).

Table 4: Pill burden in HD and PD

| Age  | HD (n) | PD (n) | Drug classes/d (HD) | Drug classes/d (PD) | p value | Total pills/d (HD) | Total pills/d (PD) | p value |
|------|-------|-------|---------------------|---------------------|---------|-------------------|-------------------|---------|
| 18-59| 39    | 36    | 7±1                 | 8±3                 | 0.007*  | 11±2              | 14±5              | 0.001*  |
| ≥60  | 19    | 16    | 8±2                 | 7±2                 | 0.033*  | 10±3              | 10±1              | 1.000†  |
| Mean | 7±2   | 8±3   | 0.033*              |                      |         | 10±3              |                   | 0.002*  |

*p<0.05 is considered statistically significant (unpaired t-test), 'NS-Not significant at the 0.05 probability level, data are given as number (n) of patients, values expressed in mean±standard deviation, Abbreviations: HD-hemodialysis, PD-peritoneal dialysis

Fig. 1a: Drug class distribution in predialysis

Fig 1a. Others include: CAD, hyperlipidemic drugs, hypothyroidism drugs, hyperthyroidism drugs, anti-emetic drugs, laxatives, hematins, uric acid inhibitors, COPD (rare patients).

Abbreviations: coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD)

Fig 1b. Others include: CAD, hyperlipidemic drugs, hypothyroidism drugs, anti-emetic drugs, laxatives, hematins, uric acid inhibitors, COPD (rare patients)

Abbreviations: coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD)
Fig. 1c: Drug class distribution in PD

Fig. 1d: Drug class distribution in RTR

Table 5: Average monthly medicinal expenditure for buying pills in CKD patients between the modalities

| Modalities   | Average medicinal expenditure (in rupees) | p-value (pre-dialysis vs HD) | Pre-dialysis vs PD | Pre-dialysis vs RTR | HD vs PD | HD vs RTR | PD vs RTR |
|--------------|------------------------------------------|------------------------------|--------------------|---------------------|--------|----------|--------|
| Pre dialysis | 2270±1000                                | 0.634†                       | 0.848†             | 0.001*              |        |          |        |
| HD           | 2195±900                                 | 0.634†                       | 0.848†             | 0.510*              | 0.001* |          |        |
| PD           | 2300±750                                 |                              |                    |                     |        |          | 0.001* |
| RTR          | 5200±2060                                |                              |                    |                     | 0.001* | 0.001*   | 0.001* |

*p<0.05 is considered statistically significant (one-way ANOVA). †NS-not significant at the 0.05 probability level, values expressed in mean±standard deviation (SD). Abbreviations: HD-hemodialysis, PD-peritoneal dialysis

DISCUSSION

Globally, CKD is becoming a major health problem for the public. Thus, patients with CKD are an ideal target for interventions aimed at reduction of morbidity and mortality. This study focused on drug classes, daily total PB and financial burden for buying medicines in different modalities in CKD patients.
CKD management contributes to significant financial burden together on health systems, patients and their households. In developing countries, such as India, kidney failure cases were increased mainly in the elderly populations [17]. In middle-income countries, the financial burden is the major concern for the people who acquire treatment for dialysis or kidney transplantation. In patients with CKD belonging to low-income countries, the morbidity and mortality rate per annum found to be high as they cannot be able to afford the treatment for kidney failure [18].

This present study data showed that CKD burden was more in the age group 18-59 y when compared to age group ≥60 y and males were more predominant than females. The etiological factor in CKD found to be DM followed by HTN, GGN, CIN, and ADPKD. We found diabetic CKD was more in the employed group while non-diabetic CKD was more in the agricultural group. Female CKD patients found to be more dependent than males. In our study, based on the modality of treatment majority of the CKD patients belong to stage 1-5 (pre-dialysis). Comorbid conditions such as cardiovascular disease (CVD), ischemic heart disease (IHD) and peripheral artery disease (PAD) have been shown to be associated with increased hospitalizations among ESRD [19, 20] and pre-dialysis patients [21] that might enhance the financial burden in these populations. Multiple factors play a key role in adherence to pharmacological therapy in CKD population. One of the barriers to non-adherence is a financial burden in this population. The link between PB to adherence and outcomes is an important role for the general population in clinical practice setting [22].

This study was focused to find out the extent of PB on patients belonging to various stages of CKD on different treatment modalities including pre-dialysis, HD, PD, post-transplant groups (RTR). With regard to PB, represented as number of pills/d we observed that it was 12±5 in pre-dialysis, 10±3 in HD, 13±5 in PD, 14±7 in RTR and we did not find any statistical difference but when compared with age groups (18-69 y and ≥60 y) also showed no significance except in PD patients. With regard to different drug classes/d, we observed that it was 7±3 in pre-dialysis, 7±2 in HD, 8±3 in PD, 9±3 in RTR and we did not find any statistical difference but when compared with age groups (18-69 y and ≥60 y) also showed no significance except in HD patients. Our observation suggests that the average PB in the number of pills/d is 12±5 (7-17 pills/d) and average PB in the number of drug classes/d is 8±3 (5-11 drug classes/d) among different modalities. A similar study was conducted in the year 2009 by Kathrine Parker et al., in the US and their study reported that HD patients had a significantly lower PB (11±7 pills/d) compared with PD patients (16±7 pills/d) [23]. A similar study was conducted in the year 2011-2012 by Uma Rani Adhikari et al., in two tertiary care hospitals, Kolkata who were running renal transplant program, their study mean PB ranged between 10-21 pills/d [24]. The pharmacological therapy varies with an average number of medicines given to different modalities. In the present study, it was found that there is a significant difference (*p<0.05) observed in average drug classes/d and average pills/d between HD and PD.

In addition to the medications that are taken in pre-dialysis, HD and PD patients, the RTR patients require immunosuppressant’s and anti-hypertensive drugs followed with other medications which are required for them were given that might contribute to more number of pills/d compared to other modalities. Majority of post renal transplantation medication include triple immunosuppressive i.e., prednisolone, mycophenolate mofetil, tacrolimus or sirolimus. Sirolimus usage was limited to patients from whom from tacrolimus was been removed for medical reasons. In a study by Kathrine Parker et al., also reported that more number of RTR patients consumes anti-hypertensive medications and hence observed more burden to consume medications in this group [23].

With regard to financial burden in the present study, all the patients were been supported for dialysis treatment indicating that there was no expenditure from the patients towards dialysis procedure. However, the financial burden for the medicinal expenditure was valuable. The CKD patients on RTR were been found to have high financial burden when compared to other modalities. Thus, from the present study it was observed that all the CKD patients were financially being supported completely for dialysis. Henceforth if likely extension of the similar support for the provision of drugs for all the CKD patients in various stages can be considered to reduce the burden on pharmaceutical costs not only for the patients but also to the caregivers of the family which increases the adherence to medications. On a cross-sectional study basis, a one-time impromptu expression on approximate expenditure they incur on monthly basis for the drugs was been considered. However, the patients do receive support in the form of reimbursement in certain of the categories and supports from charity organizations for some categories. Therefore, the information provided on the expenditure is an approximate figure.

CONCLUSION

From the present study, we conclude that the monthly medicinal costs in CKD patients with pre-dialysis, HD and PD were variable. It is observed that the CKD patients on RTR were having high financial burden/costs for medicines. Thus, measures to provide free medicines or subsidized medicines might be considered that reduce the pharmaceutical costs and increases the adherence to therapy. Keeping this observation in view in order to reduce PB, the practice of prescribing fixed drug dose combinations, extended release or sustained release formulations and the drugs with long acting agents and prescribing medicines based on their absolute indication can be the logical strategies to reduce the pill number and also drug classes. In addition to above, the practice of prescribing utilization of generic drugs may significantly reduce the expenditure on drugs, which ultimately reduce the financial burden. An additional support of Rs. 3000 to 5000 per patient would help in relieving their financial burden and indirectly encouraging them to utilize the savings to be used for family support, compliance to therapy, better nutritional support and reducing the financial burden on a patient.

This understanding would help the supporting organizations to include a fiscal consideration while planning policy issues to meet the disease treatment requirements holistically.

Limitation of the study

The main limitation of the present study was that it was been carried out only for a short duration. Adherence was not studied which remains the main problem in chronic condition patients, especially with large PB. Another main limitation was that not all healthcare cost components were included in the present study.

ABBREVIATION

- chronic kidney disease (CKD)
- hypertension (HTN)
- diabetes mellitus (DM)
- pill burden (PB)
- national kidney foundation/kidney disease outcomes quality initiative (NKF/KDOQI)
- hemodialysis (HD)
- peritoneal dialysis (PD)
- renal transplant recipient (RTR)
- mumbai kidney foundation (MKF)
- end-stage renal kidney disease (ESRD)
- chronic glomerulonephritis (CGN)
- chronic interstitial nephritis (CIN)
- autosomal dominant poly cystic kidney disease (ADPKD)

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AUTHORS CONTRIBUTIONS

1. Cirevali Pavithra had contributed in concepts, design, the definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, manuscript review.
2. Harini Devi N had contributed in concepts, definition of intellectual content, literature search, statistical analysis, manuscript preparation, manuscript editing, manuscript review.
3. Parlapalli Lalith Kumar had contributed in concepts, design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis.
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5. Kuttiappan Anitha had contributed in concepts, design, definition of intellectual content, literature search.

6. Dr. V. Siva Kumar had contributed in concepts, design, definition of intellectual content, manuscript editing, manuscript review.

CONFLICT OF INTERESTS
Declared none

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