Original Article

Role of Pharmacist Interventions in Drug Related Problem among Chronic Kidney Disease Patients

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ABSTRACT

Background: Chronic kidney disease is a longstanding disease which leads to gradual loss of kidney function causing renal failure. Although medications are more effective, Increase in the number of drugs can lead to various drug related problems. Our study aims to identify the most common DRPs in chronic kidney disease patients. **Materials and Methods:** A prospective observational study done in the Department of Nephrology, PSG Hospital, Coimbatore, India ($n=148$). The patients were regularly followed up, drug related problems were identified, reported to the physician and assessed using Pharmaceutical Care Network Europe while Naranjo scale was used to identify adverse reactions. Chi -square test was used to analyze the data. **Results:** A total of 148 patients were enrolled for the study. 62.8% males and 37.6% females. 28% were of the age group between 60-69 years while 2% were of age above 80 years. By use of Pharmaceutical Care Network Europe scale, the identified problems were categorized under treatment effectiveness (65%), others (24%) and treatment safety (11%). The most predominant drug related problem was drug interactions under treatment effectiveness. The major causes associated with the problems were found to be drug selection (28%), dose selection (22%), drug use process (22%), treatment duration (2%), others (26%). Chi-square test was used to find the correlation between stages of chronic kidney disease and poly-pharmacy, it was found to be statistically significant. Association between co-morbid conditions and drug related problems were found to be statistically significant. **Conclusion:** It is important to identify drug related problems to avoid further complications and progression of the disease. A total of 54 drug related problem were identified by reviewing medication charts. Various parameters like social habits, poly-pharmacy and co-morbid conditions have significant association with drug related problems. Therefore, healthcare professionals, caregivers and patients should work together to avoid drug related problems and improving quality of life.

Keywords: CKD, Drug-related problem, ADRs, PCNE, Poly-pharmacy.

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INTRODUCTION

Drug related problem cause preventable impact on health care results, particularly in hospitals. Studies show that in-hospital drug related problems are on higher scale in India.[1,2] Statistical reports from studies showed the increased presence of DRP prevalence in medical sectors (45%), in a group of people differentiated by the elderly, poly-pharmacy and multi-morbidity.[3] up to 40% of hospital inpatients incurred problems related to drugs, rising as the fourth - sixth main cause of death at the health care level.[3-6] A majority of ADEs and potential ADEs were classified as serious or significant and almost 5% were life-threatening. Strikingly while most potential ADEs were preventable, almost none were intercepted.[7] The most common drug classes accounting for preventable ADEs were antibiotics, followed by analgesics.[8-10]

Prevalence of DRPs were high in hospital inpatients. A lot of factors add to increased rate of prevalence, but poly-pharmacy along with advanced age has frequently

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been recognized as predominant factors of risk.[11-15] Administration of many drugs has shown to increase patient risk to ADRs, D-D interactions and medication non-compliance particularly in geriatric population.[16-18] The debate of preferring one over two factors, inappropriate drug use or advanced age as the most definitive risk factor for development of DRPs is unsolved.[19-25] Solving this issue would provide a huge relevance to medicinal practice, this could allow medical practitioners and pharmacists to provide deserving attention to patients with "true" risk factors.[26-30] A detailed study of DRPs conducted on hospital inpatients can provide much needed insights to healthcare professionals attempting to alleviate the occurrence of DRPs. By selectively monitoring patient risks, prevention of DRPs occurrence before they exist is achievable.[31-34] pharmacological drug therapy evaluation after it has been initiated is extremely important for the detection of DRPs and improving outcomes of treatment. Different studies have reported that clinical pharmacist's intervention aids to steer clear of DRPs and betters the patient's outcomes following pharmacotherapy and effectiveness of care.[11-14] On the other hand, educational intervention at discharge and follow-up of patients by clinical specialists may also prevent adverse events and can improve patients awareness of their drug therapy which in turn would improve their adherence to drug therapy.[24-27] In recent years, healthcare professionals have developed and evaluated different interventions in order to identify and solve relevant DRPs during discharge from hospital, which avoids major adverse events. Medication reconcilement and drug chart review are two ways to identify and solve DRPs at transition of care. Conducting drug reviews within or between different hospitals showed to have a beneficial impact on DRPs. Based on the available information sources, PCNE defined simple, intermediate and advanced medication reviews.[21-22] The detection of DRPs are directly linked to the types and sources of information available for medication reviews. The Extent of DRPs that can be identified and solved by reviewing the medication chart that would require a consultation with the prescriber.[9-15]

MATERIALS AND METHODS

Study population and Study Design

This prospective observational analysis was done in a multi-specialty hospital in the Nephrology Department of PSG Hospitals Coimbatore, for a period of 6 months (2021). The study was authorized by PSG Institutional Human Ethics Committee (IHEC). The sample size was calculated using Raosoft calculator with 5% margin of error, 95% confidence interval. Patient enrollment was based on inclusion criteria which includes age above 18 years, Patients with AKI, CKD, dialysis, Renal transplantation. Exclusion Criteria include Age below 18 years, pregnant women, Patients not willing to participate. Patients who gave informed consent form were enrolled for the study.

Data Collection and Baseline Variables

Baseline assessment included physical examination, measurement of creatinine clearance, body weight, height, Blood pressure. Data Collection form was designed which contains co-morbidities, lifestyle socio-demographic details, laboratory investigations; Stages of CKD were categorized based on Cockgraft-Gault equation. Drug Chart and pharmacist Interventions made. Drug related problems from each patients were recorded in the data collection form and classified based on the PCNE Scale used. ADR was measured using Naranjo Algorithm.

The scale has been divided into problems, causes, Interventions and outcome. There are three major domains in problem section, 8 domains for causes and 5 domains for interventions. Each problem has a cause. There may be more than one cause for a problem. Causes and problems together frequently leads to a few or many interventions. On the basis of the category of information required, it can be divided in two ways. If just the significant domain is used, there is sufficient data for research purpose. The sub domains are said to have importance only if and when the system is utilized for recording pharmaceutical care activities. The outcome section can be used to document if a problem has been solved. For the purpose of evaluation it is crucial to reflect if the issue has been resolved by a specific intervention that has not partially or fully been accepted by the physician and patient.

Statistical Analysis

The statistical analysis were carried out using Statistical Package for the Social Sciences 20 (SPSS). PCNE measuring tool was used to find the Medication Related Problems. The relationship between various variables like age, gender, social habits, co-morbidities, poly-pharmacy were compared with medication related problems were analyzed using chi-square test. A significance level was accepted as two tailed p-Values<0.05 with a confidence interval of 95%.

RESULTS AND DISCUSSION

Socio-demographic Details of the Sample Participants

Out of the 148 patients, Majority (28.37%) were in

the age groups between 60-69 yrs, followed by 25.67% between 50-59 years as mentioned in Table 1, Figure 1. Out of the 54 patients identified to have DRP, 37% of patients were of the age group 50-59, 25% were of the age group 60-69, followed by 18% of 70-79 age groups as mentioned in Table 2, Figure 2. Out of 148 patients, 93(62.8%) were males and 55 (37.16%) were females. Out of the 54 patient identified with DRPs, 61% were male and 38% were female as mentioned in Table 3,4 and Figure 3,4.

Clinical Characteristics

Out of 148 patients participating in the study, 38 were smokers, 14 were alcoholics, 22 were both alcoholic and smokers, and tobacco chewing and other habits. Out of the 148 patients, only 10 (8%) were with no co-morbid disease condition, 28(18.9%) were with single co-morbid condition and 110(74%) with multiple co-morbid conditions as mentioned in Table 5, Figure 5. The most common co-morbid condition was hypertension, cardiovascular disease, Diabetes mellitus, Diabetic Nephropathy and Sepsis. Out of 148 patients, 138 patients were prescribed with more than 5 drugs while only 10 patients were below 5 drugs as mentioned in Table 6, Figure 6. Based on Naranjo algorithm, Causality of ADR were classified into definite, Probable, Possible, Doubtful and results showed that 4 possible ADRs and 2 probable ADR as mentioned in Table 7, Figure 7.

PCNE Scale

Out of 148 patients, 54 patients were found to have DRPs. The DRPs detected were classified based on PCNE V8.02 criteria. Based on which 35(64.81%) problems were categorized under treatment effectiveness, 6(11.11%) under treatment safety and 13(24.07%) under others as mentioned in Table 8, Figure 8. The major cause for DRPs was found to be drug selection (27.7%), followed by drug use process (22%), Dose selection (22%), others (26%) and treatment duration (1%) as mentioned in Table 9, Figure 9. Interventions were proposed for each identified DRPs. The proposed interventions were grouped as per PCNE classification. 25(46.2%) interventions were proposed at the physician level, 11(20.37%) of the interventions at the drug level. 10(18.51%) of interventions were proposed at the patient level as mentioned in Table 10, Figure 10. Outcomes for the proposed interventions were classified based on PCNE and then quantified. 60.8% problems were totally solved, 8.69% were partially solved, 30.43% could not be solved as mentioned in Table 11, Figure 11.

Table 1: Age wise distribution (*n*=148).[1-11]

Age (years)	Number of patients	%
20-29	7	4.72
30-39	18	12.16
40-49	23	15.54
50-59	38	25.67
60-69	42	28.37
70-79	17	11.48
>80	3	2.02

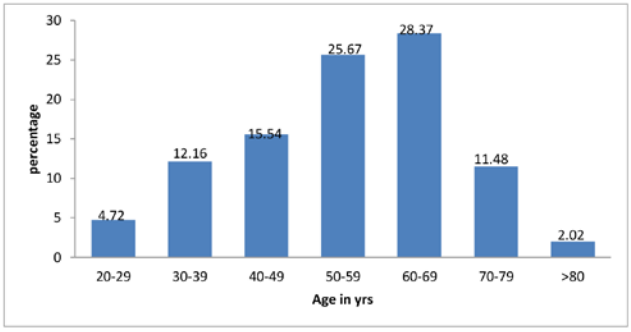

Figure 1: Age wise distribution (n=148).[1-11]

Table 2: Age wise distribution of DRPs (*n*= 54).[7]

Age (years)	Number of patients	%
20-29	2	3.7
30-39	2	3.7
40-49	5	9.2
50-59	20	37
60-69	14	25.9
70-79	10	18.5
>80	1	1.8

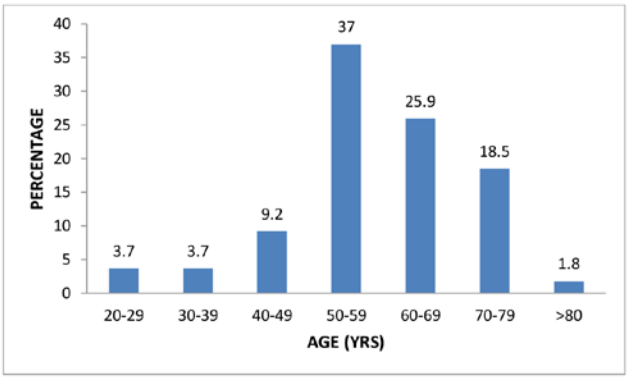

Figure 2: Age wise distribution of DRPs.[7]

Table 3: Gender wise distribution (*n*=148).[9]

Gender	Number of patients	Percentage (%)
Male	93	62.8
Female	55	37.16

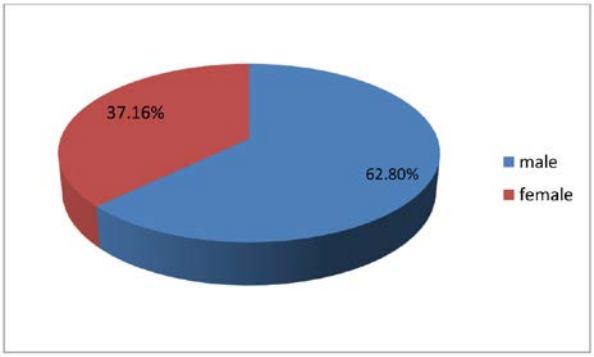

Figure 3: Gender wise distribution of DRPs (n=148).[9]

Table 4: Gender wise distribution of DRPs (*n*=54).[20]

Gender	No. of patients	Percentage(%)
Male	33	22.29
Female	21	14.18

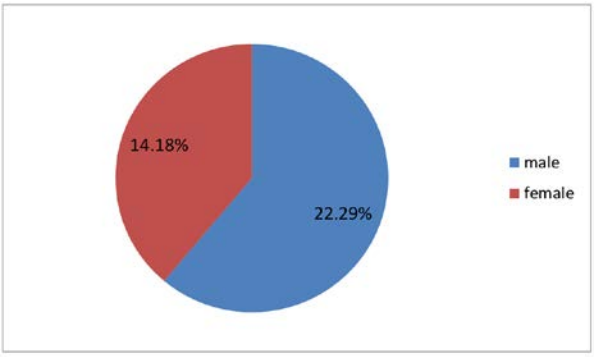

Figure 4: Gender wise distribution of study population.[20]

Table 5: Distribution of social habits in study population (*n*=148).[21]

Social habits	No. of patients	Percentage(%)
None	26	17.5
smoker	60	40.54
alcoholic	36	24.3
Alcoholic and smoker	22	14.8
Others	4	2.7

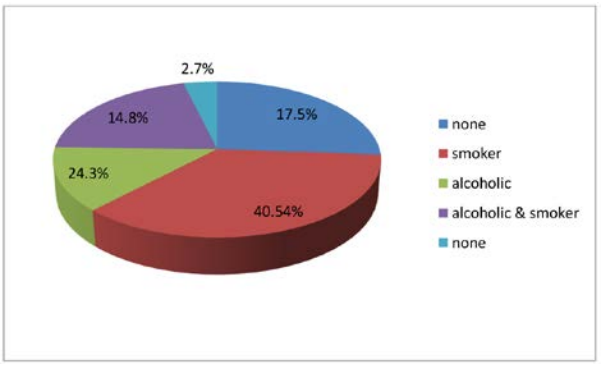

Figure 5: Distribution of social habits of study population.[21]

Table 6: Number of Drugs Prescribed (*n*=148).[22]

Number of drugs prescribed	Number of Patients	Percentage(%)
1	0	0
2-5	10	6.75
>5	138	93.24

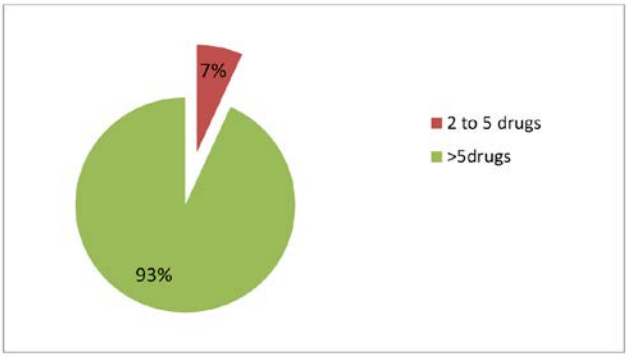

Figure 6: Number of drugs prescribed (n= 148).[22]

Table 7: Causality of ADR (N=54).[18]

Causality	Total number	Percentage(%)
Definite	-	-
Probable	2	3.70%
Possible	4	7.40%
Doubtful	-	-

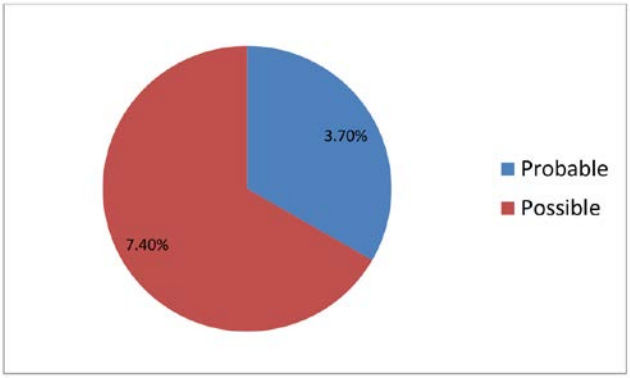

Figure 7: Causality of ADR.[18]

Table 8: Classification of DRP as per PCNE (*n*=54).[10]

Code	Problems	Number of problems	Percentage (%)
P1	Treatment Effectiveness	35	
P1.1	No effect of drug treatment	0	
P1.2	Effect of drug treatment not optimal	20	64.81%
P1.3	Untreated symptoms or indication	15	
P2	Treatment Safety	6	
P2.1	Adverse drug event(possibly) occurring	6	11.11

Table 8: Cont'd.

Code	Problems	Number of problems	Percentage (%)
P3	OTHER	13	
P3.1	Problem with cost-effectiveness of the treatment	2	24.07%
P3.2	Unnecessary drug-treatment	7	
P3.3	Unclear problems / complaints	4	

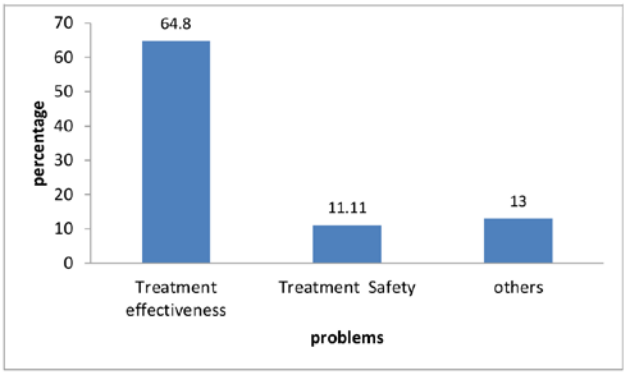

Figure 8: Distribution of DRPs.[10]

Table 9: Causes for DRPs as per PCNE classification (*n*=54).25

Code	Cause	Total number	Percentage (%)
C1	Drug Selection	15	
C1.1	Inappropriate drug according to guidelines	-	
C1.2	Inappropriate drug (within guidelines but otherwise contraindicated)	-	
C1.3	No indication for a drug	2	
C1.4	Inappropriate combination of drugs and herbal medications.	-	27.7%
C1.5	Inappropriate duplication of therapeutic group or active ingredient.	2	
C1.6	No drug treatment in spite of existing indication.	7	
C1.7	Too many drugs prescribed for an indication	4	
C2	Drug Form	0	
C2.1	Inappropriate drug form (for this patient)	-	-
C3	Dose Selection	12	
C3.1	Drug dose too low	-	
C3.2	Drug dose too high	-	
C3.3	Dosage regimen not frequent enough	3	22.22%
C3.4	Dosage regimen too frequent	2	
C3.5	Dose timing instructions wrong, unclear or missing	7	

Table 9: Cont'd.

Code	Cause	Total number	Percentage (%)
C4	Treatment Duration	1	
C4.1	Duration of treatment too short	-	2%
C4.2	Duration of treatment too long	1	
C5	Drug use Process	12	
C5.1	Inappropriate timing of administration or dosing intervals	9	
C5.2	Drug under-administered	-	22%
C5.3	Drug over-administered	-	
C5.4	Drug not administered at all	3	
C5.5	Wrong drug strength	-	
C5.6	Drug administered via wrong route	-	
C6	Patient Related	0	
C6.1	Patient uses or takes less drug than prescribed or does not take drug at all	-	
C6.2	Patient uses or takes more drug than prescribed	-	-
C6.3	Patient abuses drug (unregulated overuse)	-	
C6.4	Patient uses unnecessary drug	-	
C6.5	Patient takes food that interacts	-	
C6.6	Patient stores drug inappropriately	-	
C6.7	Patient administered drug in wrong way	-	
C6.8	Patient unable to use the drug or form as directed	-	
C7	Others	14	
C7.1	No or inappropriate outcome monitoring.	8	26%
C7.2	Other cause/ no obvious cause	6	

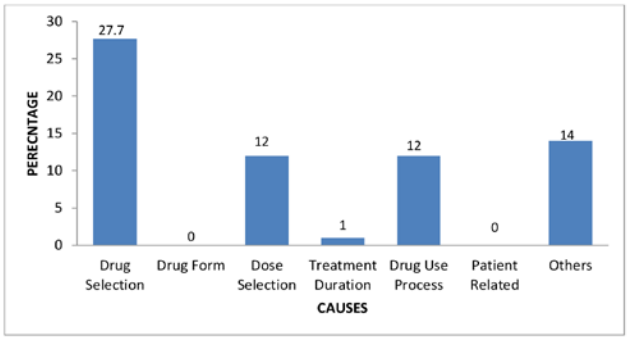

Figure 9: Causes for DRPs.[25]

Table 10: Interventions proposed for each problem(n=54).[29]

Code	Interventions	Total number	Percentage (%)
I0	No intervention	8	14.81%
I1	At prescriber level	25	
I1.1	Prescriber informed only	-	
I1.2	Prescriber asked for information	5	46.2%
I1.3	intervention proposed to prescriber	10	
I1.4	Intervention discussed with prescriber	10	
I2	At patient level	10	
I2.1	Patient(drug) counselling	4	
I2.2	Written information provided	3	18.51%
I2.3	patient referred to prescriber	1	
I2.4	Spoken to family member /caregiver	2	
I3	At drug level	11	
I3.1	Drug changed to……	1	
I3.2	Dosage changed to….	0	
I3.3	Formulation changed to…	2	20.37%
I3.4	Instructions for use changed to…	-	
I3.5	Drug stopped	3	
I3.6	New drug started	5	
I4	Other intervention or activity	-	

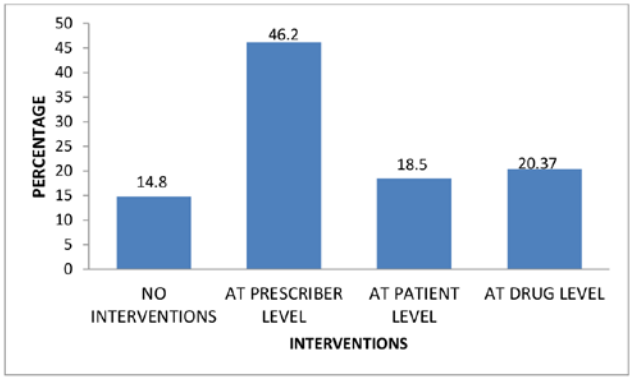

Figure 10: Interventions for the identified DRPs.[29]

Precursors to Drug-related Problems

Association of independent variables with dependent variables were investigated using chi-square test and percentage was calculated. The result shows that there is an association between social habits and DRPs with a *p*-value of 0.024, Co-morbid conditions and DRP have a *p*-value of 0.012, poly-pharmacy and DRP have a *p*-value of 0.021 which were found to be statistically significant.

Table 11: Outcomes for intervention (*n*=46).[30]

Code	Outcome for intervention	Total number	Percentage (%)
O0	Not known	0	-
O1	Problem totally solved	28	60.86%
O2	Problem partially solved	4	8.69%
O3	Not solved	14	
O3.1	Problem not solved, lack of cooperation of patient	-	
O3.2	Problem not solved, lack of cooperation of prescriber	-	30.43%
O3.3	Problem not-solved, intervention not effective	-	
O3.4	No need or possibility to solve problem	14	

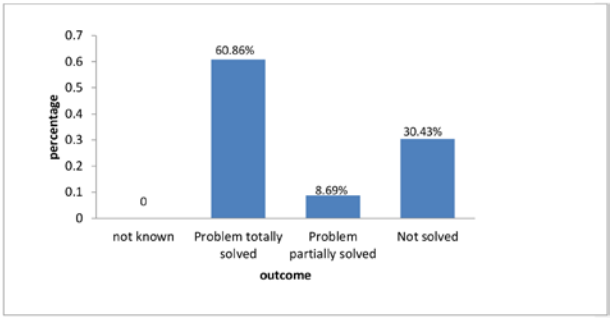

Figure 11: Outcomes for intervention.[30]

CONCLUSION

It is evident that reducing the occurrence of DRPs will lead to better outcomes for patients and reduce financial burden. As a part of health professionals, Pharmacists are best positioned to ensure that medications are used rationally due to their extensive knowledge on drug use and interactions and continuous communication with patients along with safely increasing awareness of DRPs to prevent and solve problems. The result of the present study specifically support the establish that Clinical Pharmacists through identification, prevention and resolution of DRPs are able to provide quality patient care and ultimately improve desired clinical outcomes in patients with CKD.

The nature of prospective observation in this study offers more opportunities to capture and simultaneously resolve DRPs in comparison to retrospective method. This study also justified the pharmacists ability to identify DRPs, and prevent potential DRPs and resolve actual DRPs which are vital measures to improve clinical outcomes in CKD patients.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

PCNE: Pharmaceutical Care Network European Association; **SPSS:** Statistical package for the social sciences; **DRP:** Drug related Problems; **ADR:** Adverse drug reactions.

SUMMARY

By conducting such studies, we can understand the various drug related problems in patients with multiple co-morbid conditions and polypharmacy, Provide effective solution for the same and optimize drug regimen.

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