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A PROSPECTIVE CROSS-SECTIONAL STUDY TO ASSESS THE ETIOLOGICAL PROFILE, PATIENT KNOWLEDGE AND DRUG UTILIZATION PATTERN AMONG CHRONIC KIDNEY DISEASE PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Chronic kidney disease is a condition characterized by gradual loss of kidney function over time which leads to a reduction in the glomerular filtration rate (GFR) accompanied by proteinuria. Evaluation of patient knowledge in CKD patients help to assess the degree of knowledge level regarding disease condition and assessment of drug utilization pattern helps to evaluate the various drugs used for the management of CKD and its complications. The aim of the study was to assess the etiological profile, patient knowledge and drug utilization pattern among chronic kidney disease patients. **Methodology:** This is a prospective cross-sectional study carried out among CKD inpatients in Tertiary Care Hospital, Trivandrum for a period of 6 months. A total of 110 patients were included in the study. **Results:** A total of 110 patients were analyzed during the study, of which 70% were males and 30% were females. CKD was found to mostly affect the age group of 41-60 (43.63%). Most common etiology of CKD were Hypertension (85.45%) and Type II DM (81.81%). Most common complications were anemia (86.36%) and metabolic acidosis (63.63%). Antihypertensive and diuretics were the most commonly prescribed drugs. Majority of the population were found to have an average level of knowledge (49.09%). **Conclusion:** The study demonstrated that hypertension was the major etiology and Anemia was the major complication in study population. Antihypertensive and diuretics were the most commonly prescribed drugs. Majority of the population had an average level of knowledge and moderate adherence. Analyzing the pattern of drug use and improving the knowledge and adherence helps to improve the therapeutic outcome.

KEYWORDS: CKD, Drug utilization pattern, Patient knowledge, Drug related problems.

INTRODUCTION

Chronic kidney disease is a condition characterised by gradual loss of kidney function over time which leads to a reduction in the glomerular filtration rate (GFR) accompanied by proteinuria.[1] It consists of mainly 5 stages: stage 1 (GFR 90 or higher), stage 2 (GFR 60-89), stage 3 (GFR 30-59), stage 4 (GFR 15-29), stage 5 (GFR <15). CKD is more common in people aged 65 years or older and is more prevalent in women (15%) than in men (12%).[2] The major causes of chronic kidney disease are diabetes and hypertension, which accounts for about two-thirds of the cases. HTN has been reported to occur in 85% to 95% of patients with CKD (stages 3-5).[1] Diabetic nephropathy affects 20-40 % of the individuals with diabetics, making it one of the most common complication related to diabetes.[3] Anemia is one of the major complications of Chronic Kidney Disease.[4] All these results in reduced quality of life, increased cardiovascular disease, hospitalization, cognitive impairment, and mortality.[5]

World health organization defines drug utilization study as "The marketing, distribution, prescription and uses of drugs in a society with special emphasis on the resulting medical, social and economic consequences.''[6] WHO core drug prescribing indicators are used to evaluate the drug utilization pattern in CKD patients. Patient knowledge assessment is an important aspect to evaluate the level of understanding of CKD patients regarding their disease and its management. According to a National Health and Nutrition Examination Survey (Centers for Disease Control and Prevention [CDC], 2012), among CKD patients of all age groups only around 50% of people were aware that they had the

disease, and less than 15% of people in Stages 3 and 4 CKD were aware of their kidney disease. Adherence to medication is defined as 'the extent to which the patient's behaviour matches agreed recommendations from the prescriber'. The prevalence of non-adherence to medication ranges from 17 to 74% among patients with CKD and from 3 to 80% among patients on haemodialysis, based on the various methods used to assess non-adherence.[7]

The study was conducted to assess the various etiological profile, complications, drug utilization pattern and drug related problems in CKD patients. The assessment of patient knowledge and medication adherence in CKD patients helps to evaluate the various knowledge levels of patients regarding their disease and their adherence towards the treatment provided.

MATERIALS AND METHODS
The study was a prospective cross-sectional study carried out among CKD inpatients in a Tertiary Care Hospital, Trivandrum for a period of 6 months. The subjects were chosen based on inclusion and exclusion criteria. A total of 110 patients were included in the study. A specially designed data collection form was used to gather patient information related to the study. Drug utilization was evaluated using WHO core drug prescribing indicators, Adverse drug reaction (ADR) probability was assessed using Naranjo scale and ADR severity was assessed using Hartwig ADR severity assessment scale.

Medication adherence was assessed using Medication adherence rating scale (MARS).

RESULTS AND DISCUSSION
Among the study population, 70% were males and 30% were females which showed male predominance similar to the result found in *Kamath L et al.*[8] The mean age of the study population was found to be 58.5 ± 18 years. Among the 110 subjects included in the study, majority (43.63%) of the CKD patients were in the age group 41-60, followed by 39.09% in age group 61-80, 10.90% in age group 18-40 and 6.36% in 81-100 age group.
In the study, majority of the population (85.45%) belonged to stage 5 CKD, followed by 10.90% in stage 4 CKD, 2.72% in stage 3 CKD and 0.90% in stage 1 CKD, indicating that stage 5 CKD population was the highest among study participants.

Hypertension (85.45%) (Figure 1) was the most common etiology of CKD in study, similar to the result found in *Weldegiorgis M et al.,*[9] followed by Type 2 DM (81.81%), Dyslipidemia (14.54%), Congenital anomaly (1.81%), Renal stones (0.9%), Fabry disease (0.9%) and Ig A Nephropathy (0.9%). Among the etiological profile, HTN (P=0.001), Type II DM (P=0.001), Congenital anomaly (P=0.001), Fabry disease (P=0.041) and Ig A Nephropathy (P=0.041) was found to be significant based on age. HTN was also found to be significant (P=0.025) based on gender.
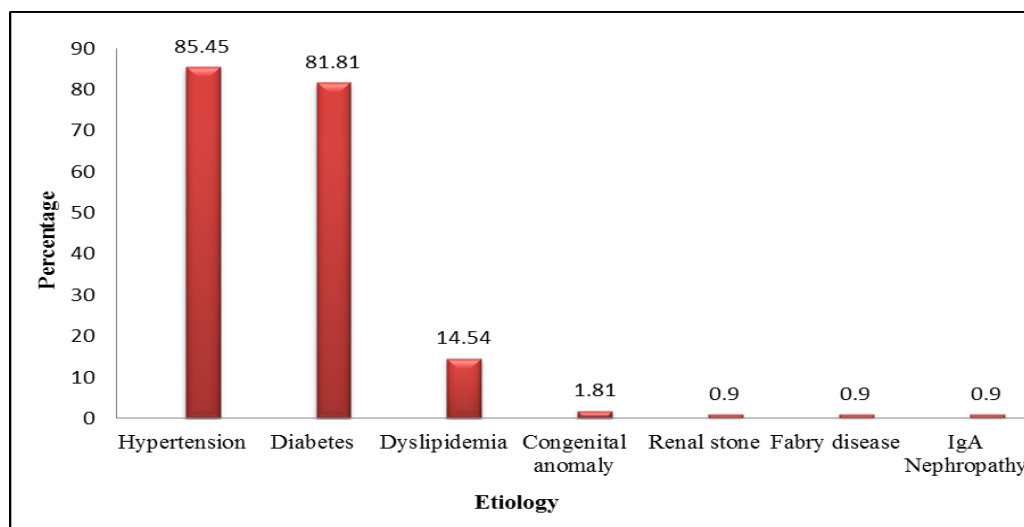

Figure 1: Etiological profile of CKD in study population.

Anemia (86.36%) (Figure 2) was the most common complication in the study population, similar to the result found in *Rajauri G et al.,*[10] followed by Metabolic acidosis (63.63%), Edema (52.72%), Hyperkalemia (43.63%) and Cardiac complications (30.9%). Among the complications, Anemia (P=0.001) and metabolic acidosis (P=0.001) were found to be significant based on age. Hyperkalemia was also found to be significant (P=0.023) based on gender.
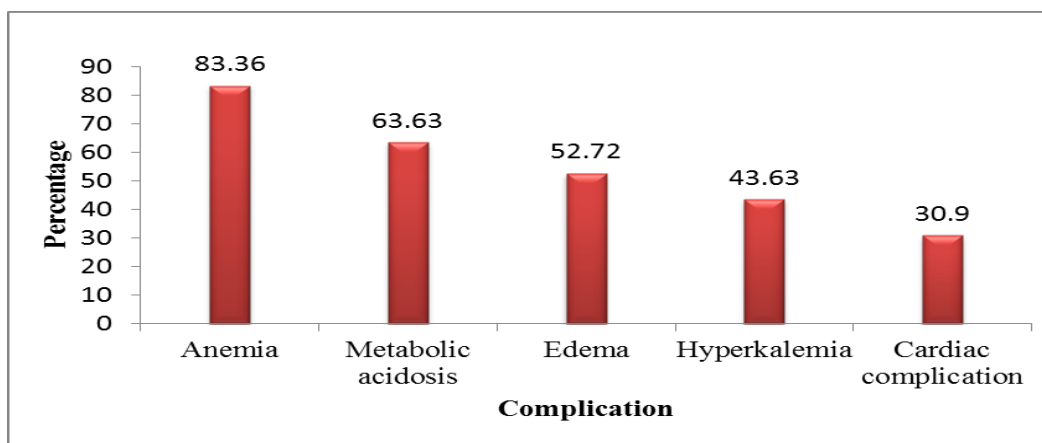
Figure 2: Complications of CKD in study population.

Antihypertensives and diuretics (20.96%) (Table 1) were the most common category of drugs prescribed in the study population, similar to that found in *Sakthirajan R et al.,*[11] followed by iron supplements (15.76%), antacids (13.72%), antibiotics (8.34%), anti-diabetics (8.44%) phosphate binders, calcium and vitamin supplements (4.82%), antihyperlipidemics (3.33%) and nutritional supplements (0.92%).

Table 1: Drug utilization pattern in study population.

DRUGS	CATEGORY	FREQUENCY	PERCENTAGE (%)
Antihypertensive and Diuretics (N=226)	Calcium channel blocker	77	34.07
	Centrally acting	20	8.84
	Beta blocker	35	15.48
	Alpha blocker	26	11.50
	Angiotensin receptor blocker	9	3.98
	Angiotensin converting enzyme inhibitors	4	1.76
	Vasopressor receptor antagonist	1	0.44
	Loop diuretics	52	23.0
	Potassium sparing diuretic	2	0.88
Anti-diabetics (N=91)	Biguanide	28	30.76
	DPP4 inhibitor	15	16.48
	Insulin	38	41.75
	SGLT2	1	1.09
	Sulfonylurea	9	9.89
Antibiotics (N=90)	Penicillin	13	14.44
	Cephalosporins	25	27.77
	Oxazolidinones	3	3.33
	Macrolides	5	5.55
	Tetracyclines	17	18.88
	Aminoglycosides	1	1.11
	Carbapenem	22	24.44
	Nitroimidazole	2	2.22
	Anti TB	2	2.22
Phosphate binder and supplements (N=52)	Sevelamer	18	34.61
	Calcitriol	10	19.23
	Calcium gluconate	11	21.15
	Cholecalciferol	2	3.84
	Vitamin K	5	9.61
	Vitamin B12	5	9.61
	Vitamin E	1	1.92
Iron supplements (N=170)	Iron phosphate	6	3.52
	Erythropoietin	51	30
	Folic acid	74	43.52
	Iron sucrose	39	22.94
Nutritional supplements (N=10)	Alfa keto analogue	10	100

Antacids (N=148)	PPI	64	43.24
	H2 Receptor Antagonist	16	10.81
	Sodium bicarbonate	63	42.56
	Sucralfate	5	3.37
Antihyperlipidemics (N=36)	Statins	36	100
Others (N=255)	Antiplatelet	39	9.41
	Anticoagulant	24	5.49
	Anticonvulsant	14	8.23
	NSAID	21	5.88
	Antiemetics	15	5.09
	Thyroid drug	13	9.80
	Analgesics	25	4.70
	Proteolytic agents	12	0.39
	Antifungal	1	2.74
	Acetylcysteine	7	1.96
	Inj Hepatitis B	5	0.39
	Prokinetic	1	4.70
	Laxatives	12	0.39
	Antipsychotic	1	2.74
	Benzodiazepines	7	6.66
	Bronchodilators	17	3.52
	Antihistamine	9	6.66
	Nitrates	17	4.31
	Anti-gout	11	1.56
	Potassium binder	4	9.41

Among antihypertensives, calcium channel blockers were the most commonly prescribed drugs (34.07%), followed by beta blocker (15.04%), alpha blocker (11.06%), centrally acting drugs (8.84%), angiotensin receptor blockers (3.98%), angiotensin converting enzyme inhibitors (1.76%), vasopressor receptor antagonist (0.44%). Among diuretics, loop diuretics were the most commonly prescribed drug (23.0%) followed by potassium sparing diuretic (0.88%). Among anti-diabetics, insulin (41.75%) was the most commonly prescribed medicine followed by biguanides (30.76%), DPP4 inhibitors (16.48%), sulfonylureas (9.89%) and SGLT2 inhibitors (1.09%). Among antibiotics, cephalosporins (27.77%) were the most commonly prescribed drug followed by carbapenem (24.44%), tetracyclines (18.88%), penicillin (14.44%), macrolides (5.55%), oxazolidinone (3.33%), nitroimidazole (2.22%), Anti-TB (2.22%), aminoglycosides (1.11%).

Among phosphate binders and calcium, vitamin supplements, sevelamer (34.61%) was the most common drug prescribed followed by calcium gluconate (21.15%), calcitriol (19.23%), vitamin k (9.61%), vitamin B12 (9.61%), cholecalciferol (3.84%), vitamin E (1.92%). Among iron supplements, folic acid (43.52%) was the most commonly prescribed drug followed by erythropoietin (30%), iron sucrose (22.94%), iron phosphate (3.52%). Among nutritional supplements, alfa keto analogue (100%) was the commonly prescribed drug. Among antacids and alkalinizing agents, proton pump inhibitors (43.24%) was the most commonly prescribed drug followed by sodium bicarbonate (42.56%), H2 receptor antagonist (10.81%), sucralfate (3.37%). Among antihyperlipidemics, statins (100%) were the most commonly prescribed category of drugs.

WHO core drug prescribing indicators (Table 2) consisting of 5 questions were used to assess the prescription pattern in study population. The average no of drugs per prescription was found to be 11, percentage of drugs prescribed by generic name was 16.86%, percentage of encounters with antibiotic prescribed was 55.45%, percentage of encounters with an injection prescribed was 90.90% and percentage of drugs prescribed from essential drug list was found to be 51.16%.

Table 2: WHO core drug prescribing indicators.

WHO PRESCRIBING INDICATORS	NUMBER	PERCENTAGE (%)
Average no of drugs per prescription	11	
Percentage of drugs prescribed by generic name	202 out of 1198	16.86
Percentage of encounters with antibiotic prescribed	61 out of 110	55.45
Percentage of encounters with an injection prescribed	100 out of 110	90.90
Percentage of drugs prescribed from essential drug list	613 out of 1198	51.16

Drug interactions (40%) (Table 3) were the most common drug related problems in CKD patients, followed by medication error (20.74%), untreated indication (12.83%), ADR (4.93%), underdosage (4.44%), improper drug selection (2.96), drug without indication (2.71%), over dosage (2.46%) and treatment duplicity (2.22%).

Table 3: Drug related problems in study population

DRP DOMAIN	DRP SUBTYPES	FREQUENCY (N=405)	PERCENTAGE (%)
Indication	Untreated indication	52	12.83
	Drug without indication	11	2.71
Effectiveness	Improper drug selection	12	2.96
	Under dosage	18	4.44
Safety	ADR	20	4.93
	Drug interaction	162	40
	Over dosage	10	2.46
	Contraindications	0	0
Others	Non adherence	27	6.66
	Treatment duplicity	9	2.22
	Medication error	84	20.74

The most common drug class associated with DRP was antihypertensives (25.38%), followed by diuretics (13.62%), antibiotics (12.07%), alkalinizing agents (11.14%), antiplatelets (7.73%), antacids (7.43%), vitamin supplements (6.81%), antihyperlipidemics (6.19%), phosphate binders (4.95%) and antidiabetics (4.64%). Among total drug interactions (40%), moderate drug interactions (78.39%) were most common in CKD patients followed by minor drug interactions (16.04%) and major drug interactions (5.55%).

The ADR causality assessment of various drugs were carried out among which, diuretics induced ADR were the most common with an average Naranjo causality assessment of 6.5±1.2 (probable), followed by antibiotics with an average causality assessment of 6.5±1.7 (probable).

The ADR severity was assessed using Hartwig severity assessment scale. The most common severity level for diuretics and antibiotics induced ADR was found to be moderate (level 3) which indicates that treatment with the suspected drug be held, discontinued, or otherwise changed, and an antidote or other treatment was required.

Patient knowledge assessment (Figure 3) was analyzed using a validated questionnaire and study population was categorized into different knowledge levels of poor (26.36%), average (49.09%) and above average (24.54%).
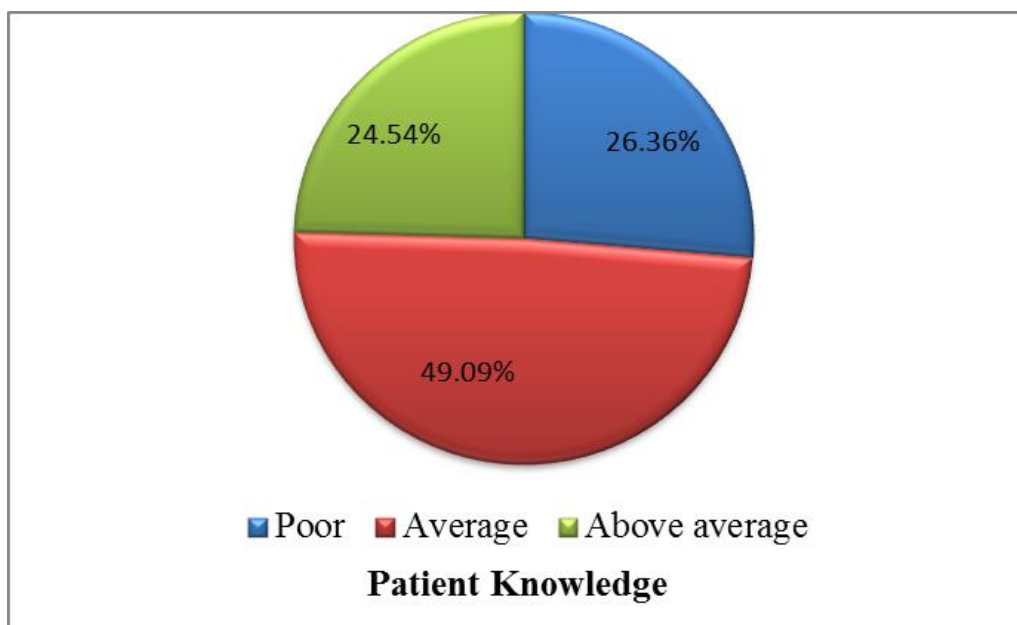

Figure 3: Patient knowledge assessment.

Medication adherence of the study population (Figure 4) was assessed using medication adherence rating scale (MARS) and categorized into low, moderate and high adherence. Majority of the study population had moderate adherence (52.72%), followed by low adherence (27%) and high adherence (25%). The result was similar to that found in *Kala T S et al.*[12] Medication adherence (Low, Moderate and High adherence) was found to be significant based on dialysis (P=0.044) and comorbid conditions (p=0.074).
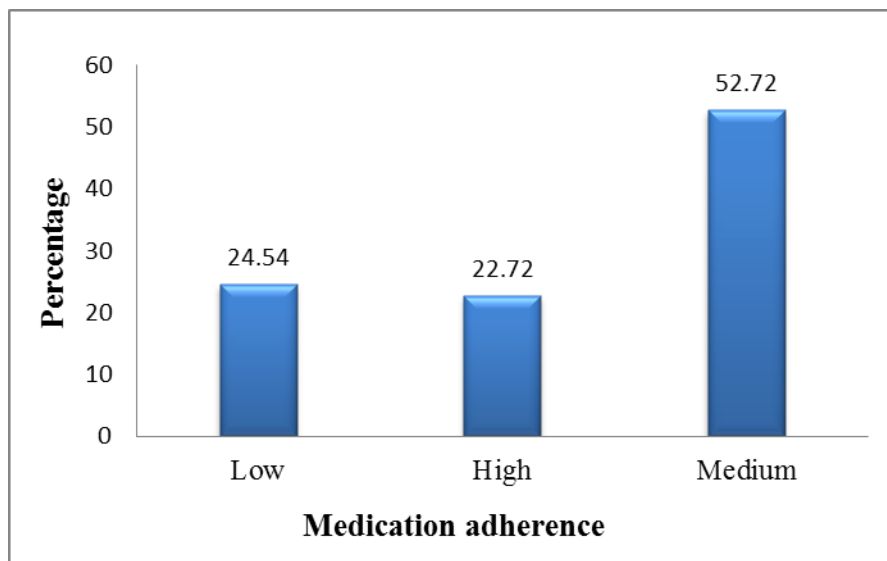

Figure 4: Medication adherence of study population.

CONCLUSION
The study demonstrated that the most common etiology of CKD was Hypertension and the most common complication of CKD was Anemia in the study population. Antihypertensives and diuretics were the most common category of drugs prescribed in the study population. Drug interactions were the most common drug related problems identified. Majority of the study population was found to have an average level of knowledge and moderate medication adherence. Analyzing the pattern of drug use and identifying, preventing and managing various drug related problems in addition to improving the knowledge levels and medication adherence helps to improve the rational prescribing pattern and therapeutic outcome.

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DECLARATION OF CONFLICTING INTERESTS
The author(s) declare no conflict of interest.

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