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ASSESSMENT OF DRUG UTILIZATION PATTERN IN CHRONIC KIDNEY DISEASE PATIENTS IN TERTIARY CARE HOSPITAL WITHOR WITHOUT SUBSTANTIAL COMORBIDITIES: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT
Background: Drug utilization studies in CKD patients help to understand and build evidence for the drug use. CKD patients have coexistence of both concordant and discordant comorbidities attributed to persisting polypharmacy, which makes it very important to study the prescribing trend on a regular basis. Objectives:The purpose of this study is to conduct a systematic review of prescription patterns, evaluate treatment compliance with standard guidelines as outlined by KDIGO, and determine evidence-based practices. We plan to develop symptom-specific questionnaires with scoring systems to track the progression and severity of the disease. Our analysis will help determine the prevalence, risk factors, comorbidities, and overall drug usage associated with chronic kidney disease as prevalence of chronic kidney disease is high, and due to lack of prescribing guidelines specific to this disease, there is significant risk of adverse reaction. Materials and Methods: An observational prospective drug utilization study was carried out in- patients of BAPS Pramukh Swami Hospital, Surat for a duration of 6 months. CKD patients fulfilling the inclusion and exclusion criteria were selected for the study and data were recorded in the CRF and formed questionnaires using patients case sheet files. Result:The study encompasses the total no of 120 patients having chronic kidney disease, of which men are found to be more prevalent than women accounting for (n=72) 60 % of the population. With regard to all age groups, those between 45 and 65 years old were the most impacted(n=66) 55%. Hypertension has been determined to be the most prevalent comorbidity, contributing to (n=113) 94.16% of all patients, contributing to the risk factors of chronic renal failure. based on formulated questionary for sign and symptoms out from different signs and symptoms such as fatigue, edema,anorexia, decreased urine output was found to be the most common and relevant sign among the all ckd stages (n=110) 91.66 %. stage G5 & G4 were higher compared to other stages due to associated risk factors such as advanced age & comorbidities with (n=84)70 % and (n=21)17.5 % respectively, contributing to highest no. of patients (n=89)74.16 % undergoing dialysis.Out of the total 998 drugs used, Antihypertensive Drugs are the most commonly used, followed by Haematinics and Drugs used for CKD such as (diuretics, drugs for acid base disorders,phosphate binders, drugs for electrolyte imbalance, and cholinergic agonist), with respective percentages of use of 21.41%, 19.42%, and 16.55%. CCBs with both reno and cardioprotective properties were the highest used antihypertensive drugs with 39.36 %. As there were many patients with end-stage renal disease, the prevalence of class diuretics was greatest overall, at 52.02% in drugs used for CKD. Conclusion: According to the results of our study, Chronic Renal Disease is primarily correlated with polypharmacy and comorbidities. The study site follows evidence-based practice along with Guidelines KDIGO.This study focused on to identifying the sign symptoms of disease based on various stages, risk factors, associated comorbiditiesand utilized drugs and it was found that males (60%) are found to be more prevalent, hypertension (94.16 %) is the most commonly found comorbid condition reflecting the highest utilization of antihypertensive drugs(21.41%)The burden of ESRD was higher due to existing comorbidities leading to increased risk of mortality and compromised renal outcome.

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INTRODUCTION

Chronic kidney disease (CKD) refers to a heterogeneous disorder characterized by kidney damage or an estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 mt2, persisting for 3 months or more, regardless of the cause.[1]If left untreated, it can lead to kidney failure, which can cause symptoms such as acidosis, anemia, volume overload, electrolyte abnormalities, mineral and bone diseases, and increasing uremia, ultimately resulting in mortality.

Multimorbidity is a significant concern when caring for CKD patients, where the coexistence of both concordant comorbidities and non-concordant conditions is associated with increased healthcare utilization, length of inpatient hospital stay, and mortality.[2]

Dialysis is one of the common and important therapies used in renal replacement therapy for patients with end-stage renal disease and a major decline in GFR. The life expectancy for a person receiving dialysis is around 5-10 years, although many live for 20-30 years. However, due to a shortage of medical facilities, lack of data on epidemiology, prevalence, incidence, and the financial crisis, the mortality rate among patients undergoing chronic dialysis in India has surged to around 175,000, with a prevalence of 129 per million population. The National Dialysis program aims to generate information on the prevalence, incidence, and causes of ESRD in patients on RRT and information on treatments and outcomes by collecting well-defined epidemiological data over many years.[3]

Drug utilization evaluation (DUE) is an effective tool for monitoring the appropriateness of the usage of various medications, which is an essential component of pharmacy service provision and clinical pharmacy practice. DUE is particularly important for evaluating and improving drug use, especially in a developing country like India where drug information is lacking, and issues like illiteracy, poverty, malpractices, prescription-free dispensing, and dominance in the healthcare and marketing fields are prominent. Conducting a DUE study is necessary to administer medications for CKD using the criteria established for therapeutic treatment. These recommendations will make it easier to prescribe medications based on the available data, raising the standard of drug usage as a whole and promoting patient improvement.
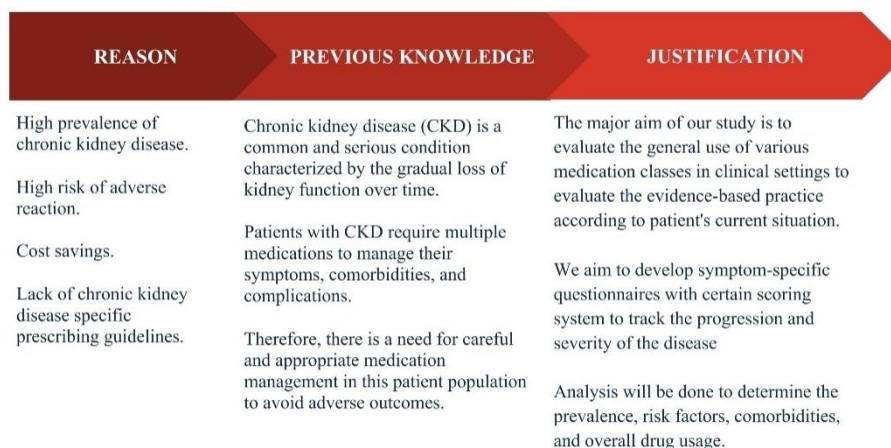
Figure 1. Study rationale.

Patients with CKD are more likely to experience drug-related problems. They need a complex therapeutic regimen requiring frequent monitoring due to various reasons: inappropriate drug use leads to adverse drug effects, increased hospital stay, and increased cost of treatment. Multimorbidity may make it more challenging for patients to maintain adherence to prescribed medications, encourage polypharmacy, and have an adverse effect on their overall quality of life. Pharmacokinetic parameters in these patients are often compromised, resulting in drug accumulation, toxicity, and adverse drug events (ADEs). Therefore, it is crucial to regularly monitor the prescription trend.

The prevalence of CKD patients has also been rising, impacting an estimated 843.6 million people globally in 2017, in part because risk factors including obesity and diabetes mellitus have become more prevalent. Each stage of CKD had a prevalence of 3.5% (stage 1), 3.9% (stage 2), 7.6% (stage 3), 0.4% (stage 4), and 0.1% (stage 5) respectively.These estimations suggest that CKD may be more prevalent than diabetes, which has been estimated to be 82% prevalent. Women are more likely than males to have CKD.[4]

The high frequency of CKD in India is caused by a number of factors. There are multiple distinct aetiologies of CKD throughout India. Stages 1, 2, and 3 of CKD were shown to have a prevalence of 13–15.04%, with 6.62%, 5.40%, and 3.02%, respectively. The reported prevalence of CKD varies by area and ranges from 1% to 13%; most recently, statistics from the kidney disease statistics Centre Study of the International Society of Nephrology revealed a prevalence of 17%. In India, there are reportedly 120,000 people receiving haemodialysis. Despite women having a larger prevalence of chronic kidney disease (CKD), adult males had a 50% higher risk of end-stage renal disease (ESRD)[5].

OBJECTIVES:
Primary objectives:
To conduct systemic review of prescription pattern monitoring.
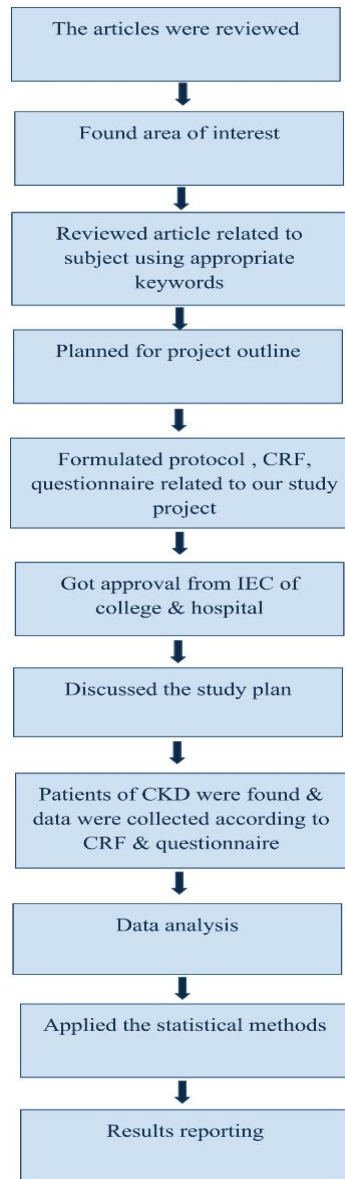To evaluate the treatment compliance with standard guidelines [KDIGO]

Secondary objectives:

To study the prevalence of chronic kidney disease based on sex and among the various age groups.

Tostudy the sign and symptoms of various stages and identifying the risk factors based on formed questionnaires.

To study the associated comorbidities in CKD patients.

To study the clinical parameters of varying stages in CKD patient.

METHODOLOGY:

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│  The articles were reviewed │
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┌─────────────────────────────┐
│    Found area of interest   │
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┌─────────────────────────────┐
│   Reviewed article related to │
│   subject using appropriate  │
│          keywords            │
└─────────────────────────────┘
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┌─────────────────────────────┐
│  Planned for project outline │
└─────────────────────────────┘
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┌─────────────────────────────┐
│  Formulated protocol , CRF,  │
│ questionnaire related to our study │
│          project             │
└─────────────────────────────┘
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┌─────────────────────────────┐
│   Got approval from IEC of   │
│     college & hospital       │
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┌─────────────────────────────┐
│    Discussed the study plan  │
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│  Patients of CKD were found &│
│ data were collected according to │
│     CRF & questionnaire      │
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┌─────────────────────────────┐
│         Data analysis        │
└─────────────────────────────┘
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│ Applied the statistical methods │
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│      Results reporting       │
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PROCEDURE :

The present study constitutes a Prospective Observational Study implemented at BAPS Pramukh Swami Hospital in Adajan, Surat, Gujarat 395009, over a six-month period from October 2022 to March 2023. The research was carried out in the nephrology department and dialysis unit, and the sample size comprised a total of 120 individuals. Patients with chronic renal disease from the nephrology department were selected, based on inclusion and exclusion criteria, to participate in the study. The relevant data was collected from the patients' case sheets. A Data Collection Form (CRF), Laboratory investigational data reports, and the eGFR-Cockcroft-Gault Calculator from the NATIONAL KIDNEY FOUNDATION were employed to collect the data. The data was subsequently analysed using MS-Excel software.

Inclusion Criteria:

- Age 18 & above with chronic kidney disease.
- Patient presented with or without substantialcomorbidities
- Patient admitted with CKD concomitant with some other medical problem.

Exclusion Criteria:
- Patients below 18 years of age.
- Pregnant women.
- Lactating women

RESULTS

Our study involved a comprehensive investigation of 120 patients, who were categorized based on several criteria, such as demographics, concordant and discordant comorbidities, risk factors, stages of chronic kidney disease (CKD), multimorbidity, creatinine clearance, and patients with and without dialysis.In order to fulfil our primary objective, we have obtained data pertaining to various classes of prescribed medications.

DEMOGRAPHIC DETAILS OF THE PATIENTS

Gender wise distribution of patients

The present study analyses a total of 120 collected samples of CKD, revealing a male predominance of n=72(60%)and a female prevalenceofn=48(40%). These findings are indicative of a higher incidence of CKD in the male population than in females.
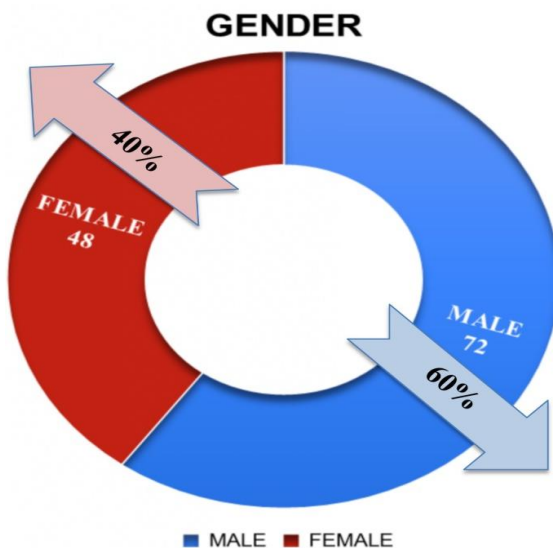
Figure 2. Gender wise distribution of study subjects.

Age wise distribution of patients

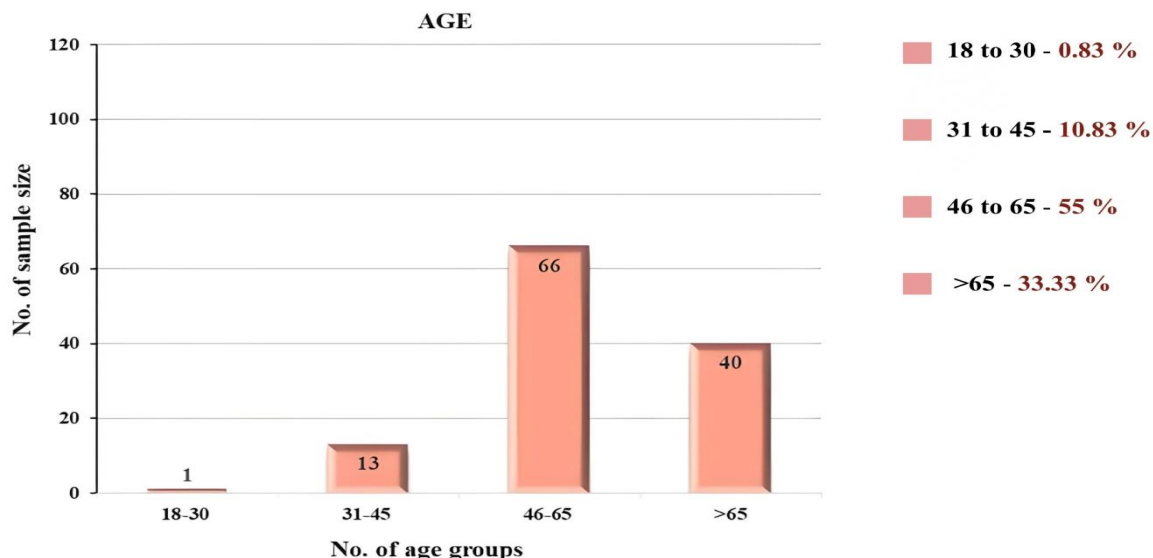| Age group	Percentage
18 to 30	0.83 %
31 to 45	10.83 %
46 to 65	55 %
>65	33.33 %

Figure 3. Age wise distribution.

Our study found that patients aged 46-65 were the most affected n=66(55%), followed by those over 65 n=40 (33.33%), and those aged 31-45 n=14 (10.83%). Patients aged 18-30 n=1 had the lowest prevalence at 0.83%.

COMORBIDITIES:
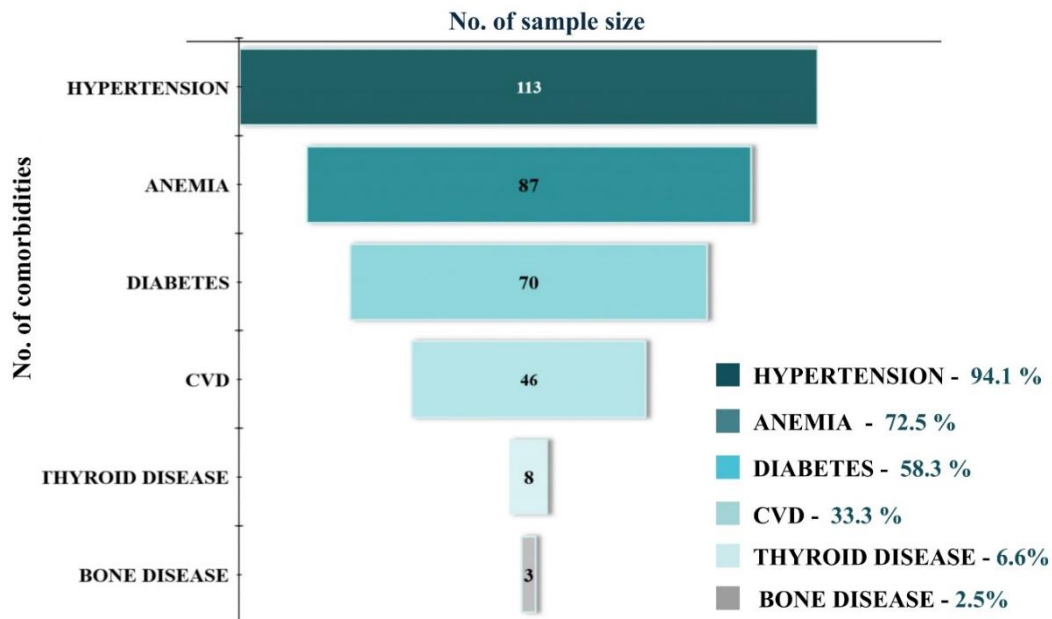**Concordant comorbidities**

Figure 4. prevalence of concordant comorbidities.

"Concordant comorbidities" refers to the presence of multiple medical conditions in an individual that are related or associated with each other. these comorbidities tend to occur together more frequently than would be expected by chance alone. A total of 120 patients suffering from at least one comorbidity are listed. Hypertension as a comorbidity is the highest among all with n=113 (94.16 %) in 120 patients.

Cardiovascular comorbidities :
Among 46 patients, the greatest CVD comorbidity rate is ischemic heart disease at 67.3%. Dyslipidemia contributes 10.9%, LV dysfunction 8.6%, stroke 6.5%, congestive cardiacfailure 4.34%, and MVR 2.1%.
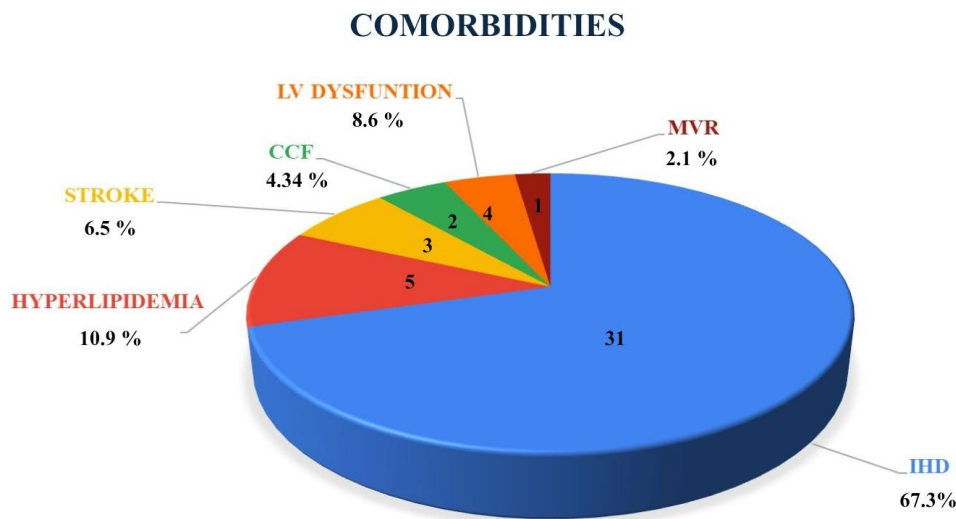

Figure 5 . cardiovacular comorbidity.

Discordant Comorbidities :

Table 1. discordant comorbidities.

DISCORDANT COMORBIDITIES (N=20)	NO. OF DISCORDANT COMORBIDITIES (N=20)	PERCENTAGE (100%)
PARKINSON	2	10%
SEIZURE	2	10%
DVT	2	10%
BPH	2	10%
DEPRESSION	1	4.7%
ALZHEIMER	1	4.7%
DEMENTIA	1	4.7%
DERMATITIS	1	4.7%
ASCITES	1	4.7%
URINARY SARCOMA	1	4.7%
COPD	1	4.7%
ASTHMA	1	4.7%
CHRONIC LIVER DISEASE	1	4.7%
ANXIETY DISORDER	1	4.7%
SYSTEMIC LUPUS ERYTHEMATOSUS	1	4.7%
HEPATOBILIARY SEPSIS	1	4.7%

"Discordant Comorbidities" typically refer to the presence of two or more comorbid conditions that are not commonly associated with each other or are not expected to occur together in the same individual based on typical disease patterns or physiological mechanisms.The following is a comprehensive list of various discordant comorbidities that were found in the 120 observed patients with chronic kidney disease (CKD).

Multimorbidity

Multimorbidity emphasizesthe simultaneous presence of multiple chronic illnesses that may or may not be related to each other.According to the results of our study, a total of 68 individuals out of the 120 surveyed (56.66%) were found to have a comorbidity of hypertension and diabetes. These findings provide valuable insights into the prevalence of these conditions.
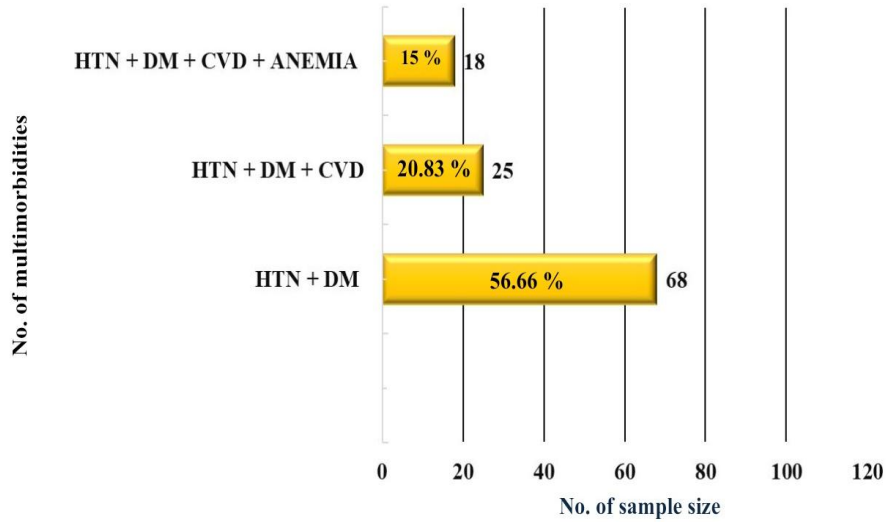
Figure6. Multimorbidity.

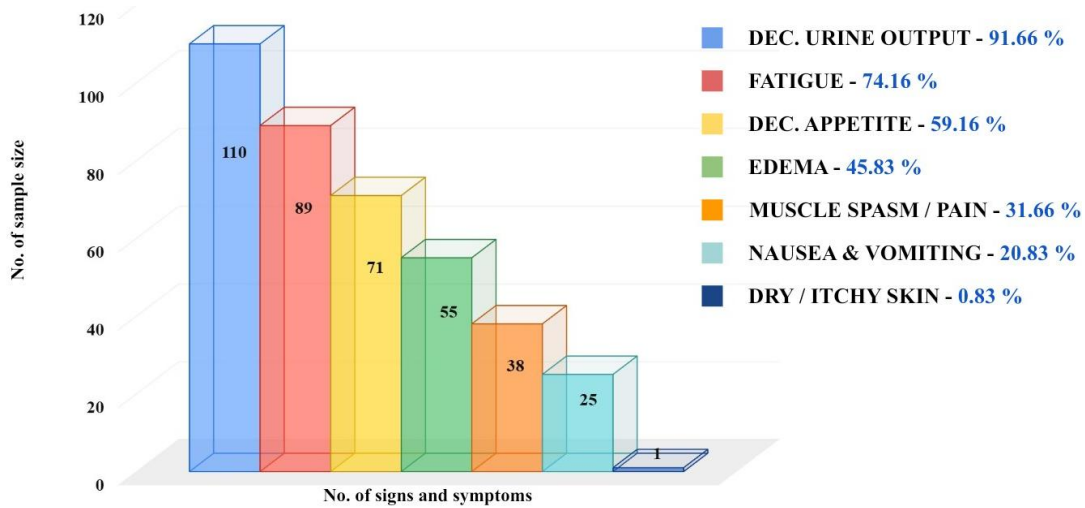**Assessment of sign and symptoms:**

Figure 7. signs and symptoms of CKD.

With 91.66% of 110 patients reporting it, decreased urine production was the most common among 120 subjects enrolled.

Risk Factors:

Among various risk factors such as older age, low birth weight and family history of kidney disease, smoking, obesity, hypertension, diabetes mellitus, (comorbidities) are considered to be strong risk factors for chronic kidney disease. The major 4 risk factors were considered in the study and Comorbidities are the major risk factors for illness development, contributing 63.78 percent of the time.
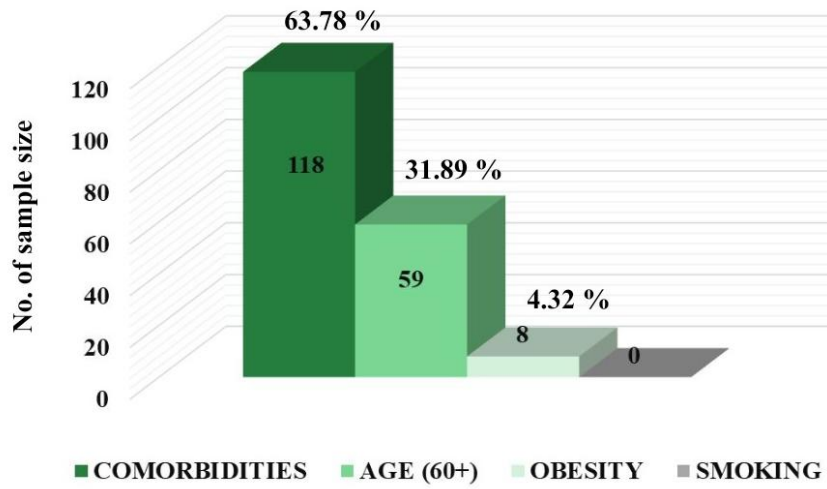
Figure 8. Risk factors.

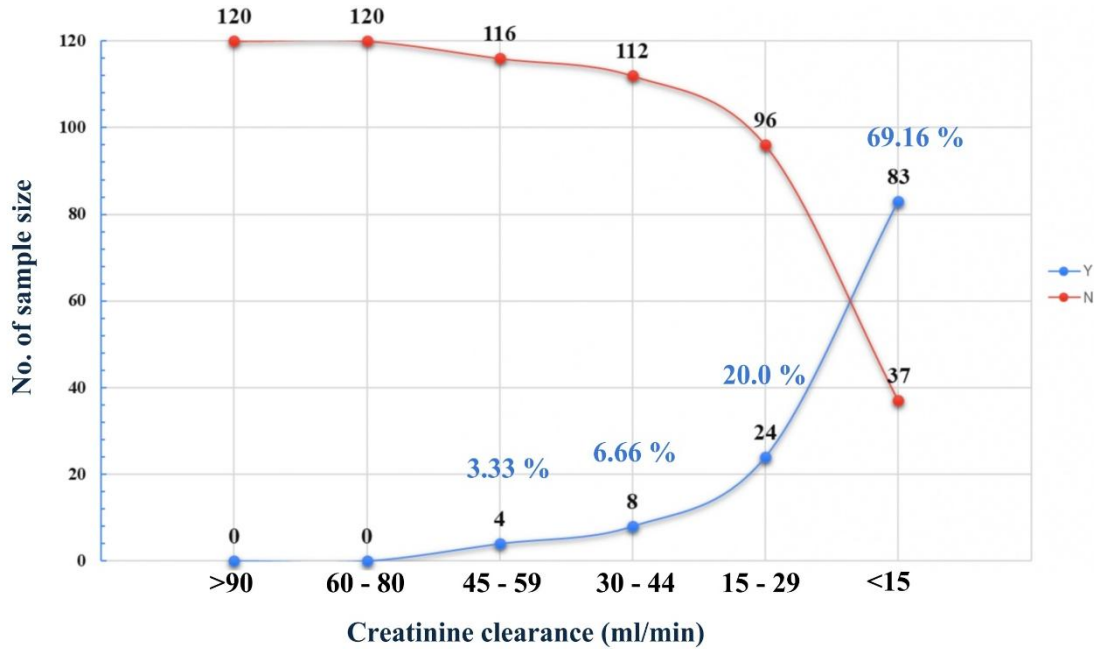**5. Creatinine Clearence:**

Figure 9. Data on creatinine clearance.

The graph clearly presents the correlation between the range of creatinine clearance rate in ml/min and the number of patients with a specific range of creatinine clearance. A decrease in the range of creatinine clearance is directly proportional to the increase in the number of patients with that clearance range, pointing towards a higher prevalence of end-stage chronic renal failure.

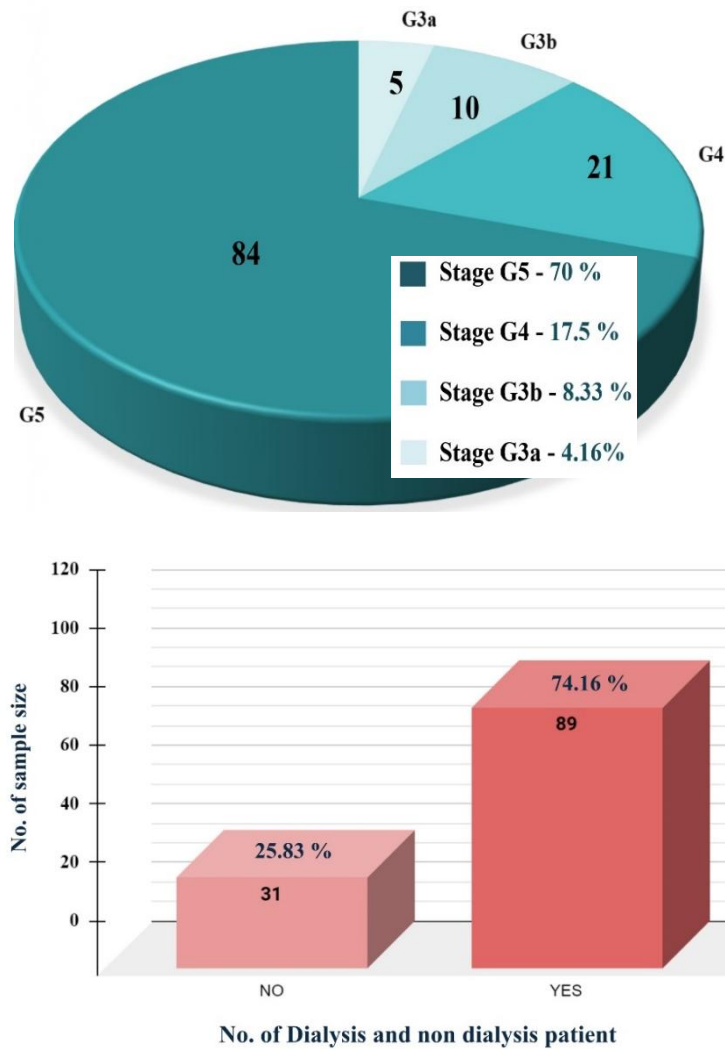**6. Assessment of Stages and No. of dialysis patients**

Figure 10. Assessment of stages and no of patients on dialysis.

Out of 120 patients enrolled in study 74. 16 % patients are undergoing dialysis which clearly indicates the higher no. of patients suffering from end stage renal disease which is correlating the highest no of patients in stage G5 n= 84 (70 %).
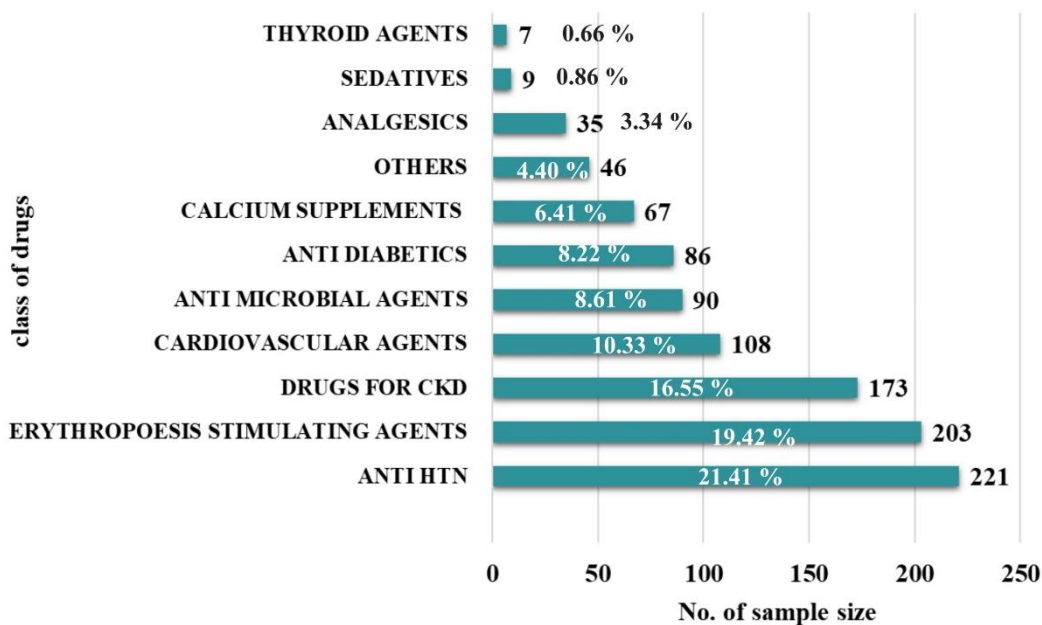
7. DRUG UTILIZATION EVALUATION

Figure 11. Drug utilization evaluation.

Total number of utiliseddrugs are n= 1045. Among the overall utilized drugs, Antihypertensives and ESAs were the most frequently used drugs, with usage rates of 21.41% and 19.42%, respectively.

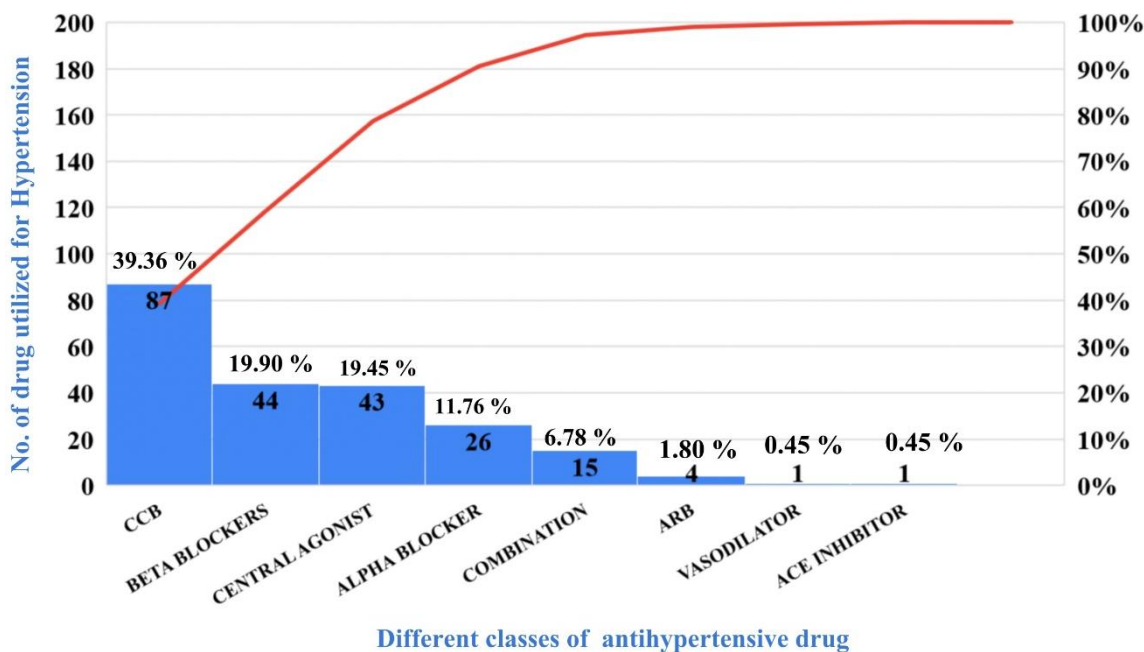**7.1 Utilization of Antihypertensive Drugs**

Figure 12. Utilization of antihypertensive drugs.

Table 2. Utilization of different classes of antihypertensive drugs.

DRUG CLASS	FREQUENCY	PERCENTAGE
CALCIUM CHANNEL BLOCKERS (n=87, 39.36 %)		
NIFEDIPINE	62	71.16 %
AMLODIPINE	11	12.64 %
CILNIDIPINE	6	6.89 %
NICARDIPINE	5	5.74 %
EFONIDIPINE	2	2.29 %
AZELNIDIPINE	1	1.14 %
BETA BLOCKERS (n=44, 19.90 %)		
METOPROLOL	23	52.27 %
CARVEDILOL	11	25%
BISOPROLOL	7	15.90%
LABETALOL	2	4.54 %
NEBIVOLOL	1	2.27%
CENTRAL AGONIST (n=43, 19.45 %)		
CLONIDINE	37	86.04 %
MOXONIDINE	6	13.95 %
ALPHA BLOCKER(n=26, 11.76 %)		
PRAZOSIN	25	96.15%
TAMSULOSIN	1	3.84%
COMBINATION OF ANTIHYPERTENSIVE AGENTS(n=15, 6.78%)		
METOPROLOL+AMLODIPINE	5	33.33%
LOSARTAN + AMLODIPINE	1	6.66%
TELMISARTAN + CHLORTHALIDONE	1	6.66%
VALSARTAN + SACUBITRIL	1	6.66%
TELMISARTAN + METOPROLOL	1	6.66%
CILNIDIPINE + TELMISARTAN	1	6.66%
ATENOLOL + NIFEDIPINE	1	6.66%
BENIDIPINE HCL + METOPROLOL SUCCINATE	1	6.66%
TELMISARTAN + HYDROCHLOROTHIAZIDE	1	6.66%
TELMISARTAN + AMLODIPINE	1	6.66%

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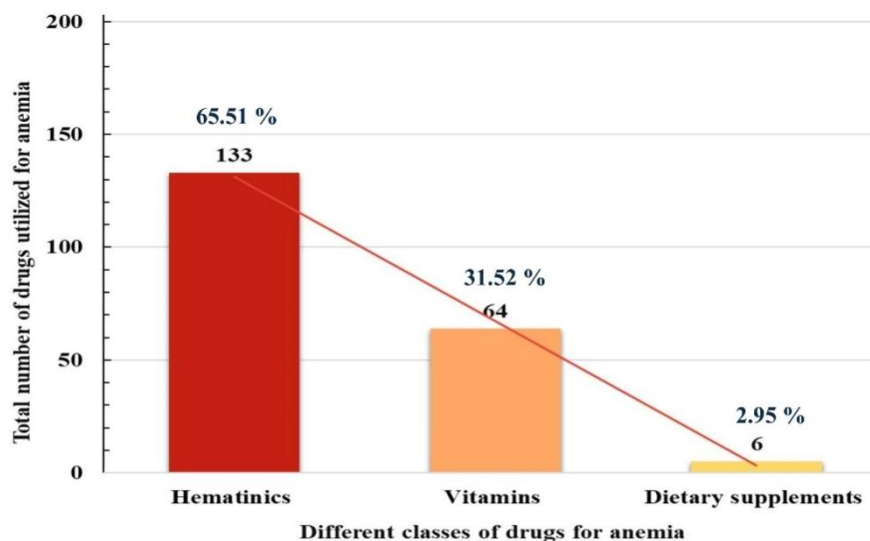| ANGIOTENSIN RECEPTOR BLOCKER (n=4, 1.80%)		
TELMISARTAN	4	100%

7.2 Utilization of Erythropoietin Stimulating Agents

Figure 13. Utilization of Erythropoietin Stimulating Agents.

Table 3. Utilization of different classes of Erythropoietin Stimulating Agents.

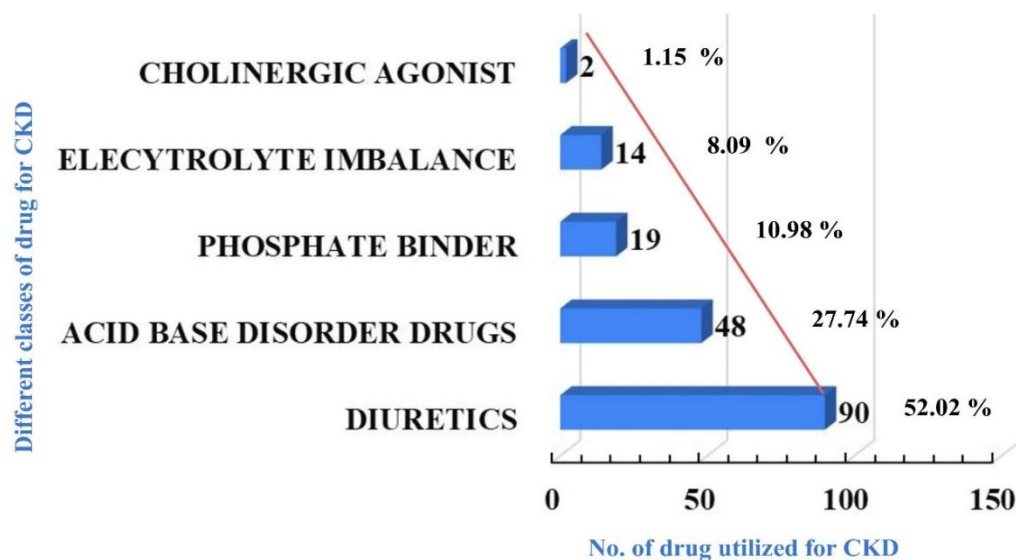| DRUG CLASS	FREQUENCY	PERCENTAGE
HEMATINICS (n=133, 65.51 %)		
ERYTHROPOIETIN ALFA	57	42.85 %
IRON SUCROSE	38	28.57%
PCV	17	12.78 %
ELEMENTAL IRON	8	6.01 %
FOLIC ACID	6	4.51 %
RECOMBINANT HUMAN ERYTHROPOIETIN ALFA	4	3 %
DARBEPOETIN ALFA	2	1.5 %
DESIDUSTAT	1	0.75%
VITAMINS (n= 64, 31.52 %)		
VITAMIN B COMPLEX	56	87.5 %
IRON + FOLIC ACID + VITAMIN B COMPLEX	8	12.5 %
DIETARY SUPPLEMENTS (n= 6, 2.95 %)		
ALPHA KETOANOLOGUE	3	50 %
FLEXIPRO	1	16.67 %
THREPTIN BISCUIT	1	16.67 %
NEPHRO H POWDER	1	16.67 %

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7.3 Utilization of Dugs for CKD

Figure 14. Utilization of drugs for CKD.

Table 4. Utilization of different classes of drugs for CKD.

DRUG CLASS	FREQUENCY	PERCENTAGE
DIURETICS (n=90, 52.02 %)		
TORSEMIDE	40	44.44 %
FUROSEMIDE	33	36.67 %
METOLAZONE	15	16.66 %
SPIRONOLACTONE	1	1.12 %
SPIRONOLACTONE + TORSEMIDE	1	1.12 %
DRUGS FOR ACID BASE DISORDER (n=48, 27.74 %)		
SODIUM BICARBONATE	29	60.41 %
FEBUXOSTAT	19	39.58 %
PHOSPHATE BINDER (n=19, 10.98 %)		
CALCIUM ACETATE	12	36.81 %
SEVELAMER	7	63.15 %
DRUGS FOR ELECTROLYRE IMBALANCE (n=14 , 8.09 %)		
K BIND SACHET	10	71.42 %
TOLVAPTAN	3	21.4%
POTASSIUM CHLORIDE	1	7.14%
CHOLINERGIC AGONIST (n=2, 1.15%)		
BETHANACHOL	2	1.15 %

7.4 Utilization of CVD agents

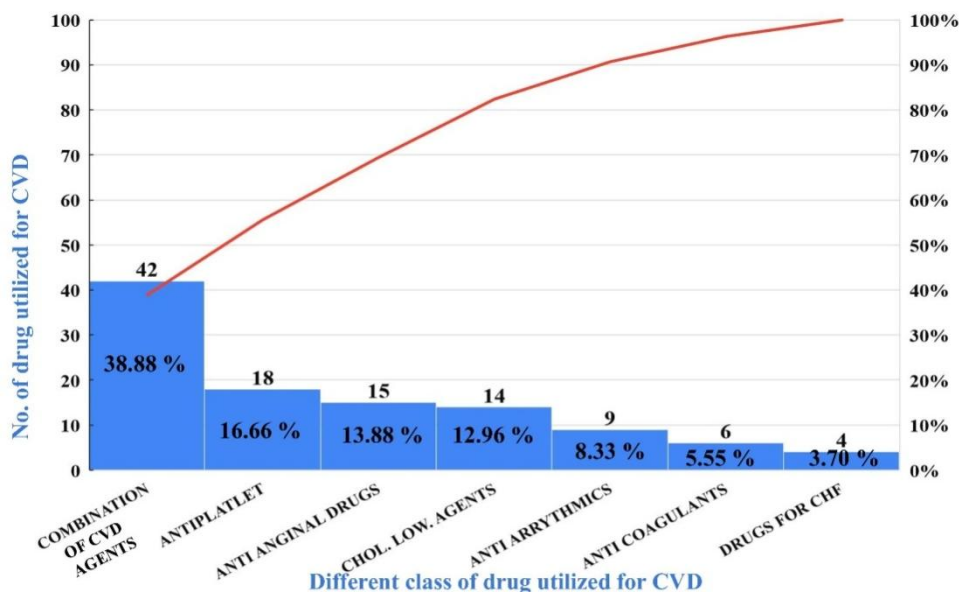**Figure 15. Utilization of CVD drugs.**

Table .5 Utilization of different classes CVD drugs.

DRUG CLASS	FREQUENCY	PERCENTAGE
COMBINATION OF CVD AGENTS (n=42, 38.89 %)		
ASPIRIN + ATORVASTATIN	23	54.76 %
ASPIRIN + ATORVASTATIN + CLOPIDOGREL	10	23.8 %
ROSUVASTATIN + ASPIRIN	2	4.76 %
ISOSORBIDE DINITRATE + HYDRALAZINE HCL	2	4.76 %
ASPIRIN + ROSUVASTATIN + CLOPIDOGREL	1	2.3 %
ROSUVASTATIN + CLOPIDOGREL	1	2.3 %
ASPIRIN + PRASUGREL	1	2.3 %
SACUBITRIL + VALSARTAN	1	2.3 %
ASPIRIN + CLOPIDOGREL	1	2.3 %
ANTI PLATELET DRUGS (n=18, 16.67 %)		
ASPIRIN	10	55.56 %
CLOPIDOGREL	6	33.3 %
TICAGRELOR	2	11.11 %
ANTI ANGINAL DRUGS (n=15, 13.88 %)		
NITROGLYCERIN	11	73.33 %
NICORANDIL	2	13.33%

ISOSORBIDE MONONITRATE	1	6.67%
RANOLAZINE	1	6.67 %
CHOLESTEROL LOWERING AGENTS (n=14, 12.96 %)		
ATORVASTATIN	12	85.71 %
ROSUVASTATIN	2	14.28 %
ANTI ARRYHTHMIC DRUGS (n=9, 8.33 %)		
AMIODARONE	6	66.66 %
DIGOXIN	3	33.33 %
ANTI COAGULANT (n=6, 5.56 %)		
ENOXAPARIN	4	66.66 %
APIXABAN	2	33.33 %
DRUGS FOR CHF	**(n=4, 3.70 %)**	
IVABRADINE	2	50 %
DOBUTAMINE	1	25 %
VERICIGUAT	1	25 %

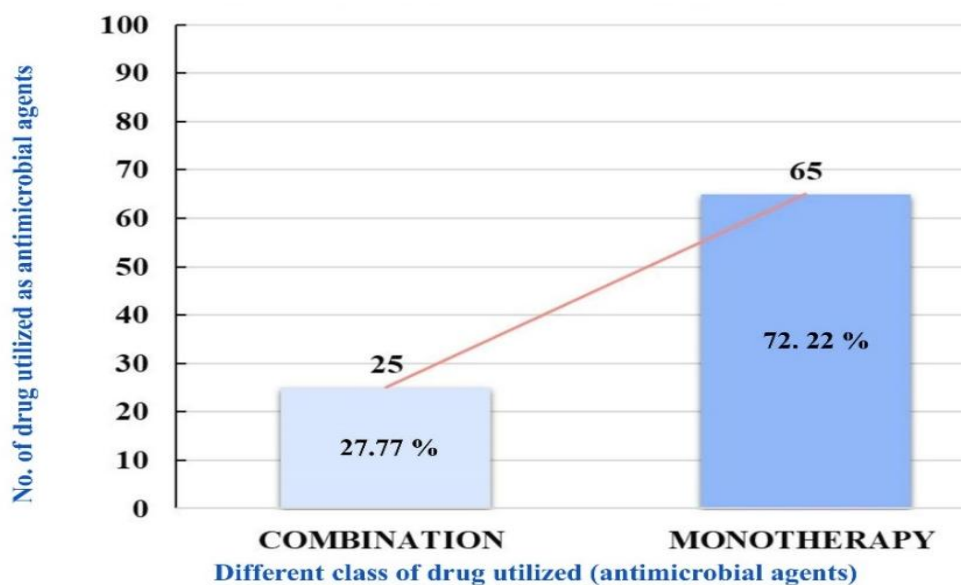**7.5 Utilization ofAntimicrobial Agents**

Figure 16. Utilization of antimicrobial agents (monotherapy vscombination).

Table 6. Utilization of different classes of antimicrobial agents (monotherapy&combination).

DRUG CLASS	FREQUENCY	PERCENTAGE
MONOTHERAPY (n=65, 72.22 %)		
CEFTRIAXONE	10	15.38 %
LEVOFLOXACIN	10	15.38 %
AZITHROMYCIN	7	10.76 %
CEFIXIME	7	10.76 %
LINEZOLID	6	9.23 %
VANCOMYCIN	5	7.69 %
MEROPENEM	5	7.69 %
METRONIDAZOLE	4	6.15 %
OSELTAMIVIR	2	3.07 %
FLUCONAZOLE	2	3.07 %
ARTESUNATE	1	1.53 %
OFLOXACIN	1	1.53 %
COLISTIMETHATE SODIUM	1	1.53 %
TARGOCID	1	1.53 %
VORICONAZOLE	1	1.53 %
CEFOTAXIME	1	1.53 %
SULTAMICILLIN	1	1.53 %
COMBINATION THERAPY (n=25 , 27.77 %)		
CEFOPERAZONE + SULBACTAM	16	64 %
PIPERACILLIN + TAZOBACTAM	4	16 %
CEFTRIAXONE + SULBACTAM	2	8 %
CEFIXIME + CLAVULANIC ACID	1	4 %
CEFTRIAXONE + TAZOBACTAM	1	4 %
CEFEPIME + TAZOBACTAM	1	4 %

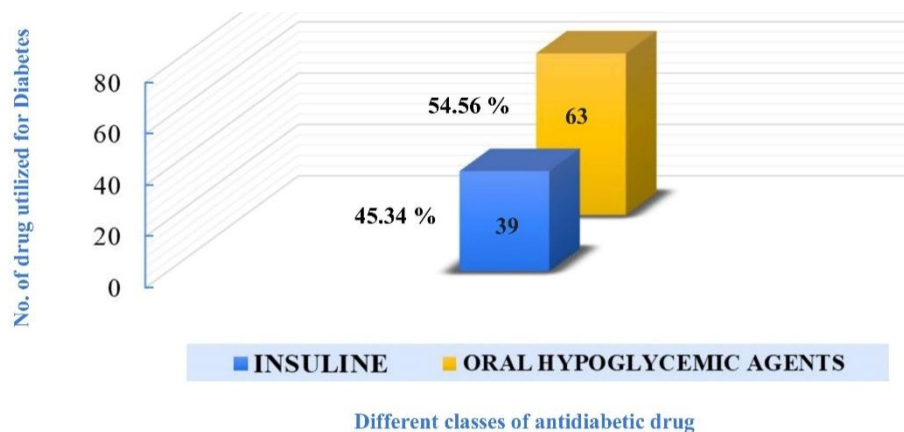**7.6 Utilization ofAntidiabetic Agents**

Figure 17. Utilization of antidiabetic agents.

17. Utilization of antidiabetic drugs

Table 7. Utilization of different classes of antidiabetic drugs.

DRUG CLASS	FREQUENCY	PERCENTAGE
ORAL HYPOGLYCEMIC AGENTS (n= 63, 54.56 %)		
DPP4 INHIBITORS	**(n=28)**	**32.55 %**
TENELIGLIPTIN	26	92.85 %
VILDAGLIPTIN	2	7.14 %
COMBINATION	**(n=8)**	**9.30 %**
GLIMEPIRIDE + METFORMIN	3	37.5 %
REPAGLINIDE + VOGLIBOSE	2	25 %
SITAGLIPTIN + METFORMIN	1	12.5 %
GLICLAZIDE + METFORMIN	1	12.5 %
DAPAGLIFLOZIN + VILDAGLIPTIN	1	12.5 %
ALPHA GLUCOSIDASE INHIBITORS	(n=5)	
ACARBOSE	5	5.81 %
MEGLITINIDES	(n=4)	
REPAGLINIDE	4	4.6 %
SGLT2 INHIBITORS	(n=2)	
DAPAGLIFLOZIN	2	2.3 %
INSULINES (n=, 27.74 %)		
H. ACTRAPID	31	79.48 %
INSULIN GLARGINE	3	7.68 %

H. MIXTARD	2	5.12 %
INSULIN	2	5.12 %
INSULIN GLULISINE	1	2.56 %

7.7 Utilization ofCalcium Supplements

Table 8. Utilization of calcium supplements (monotherapy and combination).

DRUG CLASS	FREQUENCY	PERCENTAGE
MONOTHERAPY (n=34, 50.74 %)		
CALCITRIOL	21	61.76 %
VITAMIN D3	4	11.76 %
CALCIUM GLUCONATE	4	11.76 %
CALCIUM CARBONATE	2	5.88 %
CALCIUM SACHET	1	2.94 %
TERIARATIDE	1	2.94 %
CALCIUM ASPARTATE	1	2.94 %
COMBINATION THERAPY (n=33 , 49.25 %)		
CALCIUM + VIT D3	24	72.72 %
CALCIUM CARBONATE + VITAMIN D3	4	12.12%
CALCIUM + VIT D	3	9.09%
CALCITRIOL + CALCIUM + ZINC	1	3.03%
CALCITRIOL + ELEMENTAL CALCIUM	1	3.03%

7.8Utilization ofother utilized agents

Table 9. Utilization of other utilized drugs.

DRUG CLASS	FREQUENCY	PERCENTAGE
DRUGS UTILIZED FOR BPH(n=11, 23.91 %)		
TAMSULOSIN	3	27.27 %
TAMSULOSIN + DUTASTERIDE	3	27.27 %
SILODOSIN	2	18.18 %
SILODOSIN + DUTASTERIDE	2	18.18 %
DUTASTERIDE	1	9.09 %
DRUGS FOR RESPIRATORY (n=10 , 21.73 %)		

NEB.DUOLIN + BUDECORT	3	30 %
MONTELUKAST + FEXOFENADINE	2	20 %
CHLORPHENIRAMINE + PCM + PHENYLEPHRINE	1	10 %
ETOFYLLINE + THEOPHYLLINE	1	10 %
NEB. DUOLIN	1	10 %
DEXTROMETHORPHAN HYDROBROMIDE	1	10 %
ACEBROPHYLLINE	1	10 %
ANTILEPTIC DRUGS (n=8, 17.39 %)		
LEVETIRACETAM	5	62.5 %
PIRACETAM	1	12.5 %
CARBAMAZEPINE	1	12.5 %
VALPROIC ACID	1	12.5 %
ANTIDEPRESSANTS (n=7, 15.21 %)		
QUETIAPINE	3	48.85 %
HALOPERIDOL	1	14.28 %
DULOXETINE	1	14.28 %
MIRTAZAPINE	1	14.28 %
ESCITALOPRAM + CLONAZEPAM	1	14.28 %
STEROID (n= 6, 13.04 %)		
PREDNISOLON	3	50 %
HYDROCORTISONE	2	33.33 %
DEFLAZACORT	1	16.66 %
DURGS ACTING ON URINARY BLADDER (n=3, 6.52%)		
TOLTERODINE	1	33.33 %
SOLIFENACIN	1	33.33 %
MIRABEGRON	1	33.33 %
DRUGS FOR ASCITES	**(n=1 . 2.17 %)**	
H. ALBUMIN	1	2.17 %

7.9 Utilization ofAnalgesics

Table. 10 Utilization of analgesics drugs (monotherapy & combination).

DRUG CLASS	FREQUENCY	PERCENTAGE
MONOTHERAPY (n=22, 62.85 %)		

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PCM	12	54.54 %
TRYPSIN CHYMOTRYPSIN	4	18.18 %
GABAPENTIN	2	9.09 %
DEXAMETHASONE	2	9.09 %
CONTRAMAL	2	9.09 %
COMBINATION THERAPY (n=13 , 37.14 %)		
TRAMADOL HCL + ACETAMINOPHEN	4	30.76 %
PREGABALIN + METHYLCOBALAMIN	3	23.07 %
PCM + CONTRAMAL	2	15.38 %
TRAMADOL + PCM	1	7.6 %
PREGABALIN + NORTRIPTYLINE + MECOBALAMIN	1	7.6 %
PREGABALIN + NORTRIPTYLINE	1	7.6 %
DICLOFENAC + PCM	1	7.6 %

7.10 Utilizationof Sedatives

Table 11. Utilization of sedative drugs.

DRUG CLASS	FREQUENCY	PERCENTAGE
SEDATIVES (n=9, 0.86 %)		
CLONAZEPAM	4	44.4 %
ALPRAZOLAM	2	22.2 %
SERTRALINE	1	11.1 %
AMITRIPTYLINE	1	11.1 %
CARBAMAZEPINE	1	11.1 %

7.11 Utilization of Drugs for thyroid management

Table 12. Utilization of drugs for thyroid management

| DRUG CLASS	FREQUENCY	PERCENTAGE
DRUGS UTILIZED FOR THYROID MANAGEMENT (n=7, 0.66 %)		
THYROXINE	6	85.71 %
LEVOTHYROXINE	1	14.28 %

Q – SCOREEVALUATION
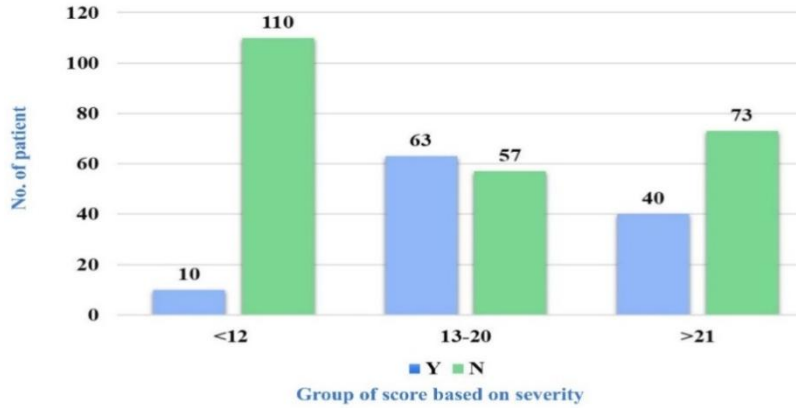
Figure 18. Evaluation of Q- Score.

The signs and symptoms were identified in the patient with questionnaires formulated by our group, where particular score was awarded to fetch the result of the same. Some symptoms are common in CKD as well general diseases are given with the score +1. Some symptoms are closely related to CKD, are given with the score +2. Comorbidities are the major risk factors of CKD, which are given with the score +5. The highest no. of patients are covered in score between 13-20 (n=63) indicating the presence of multiple symptoms closely related to CKD and end stage renal disease.

CORRELATION BETWEEN AGE AND COMORBIDITIES
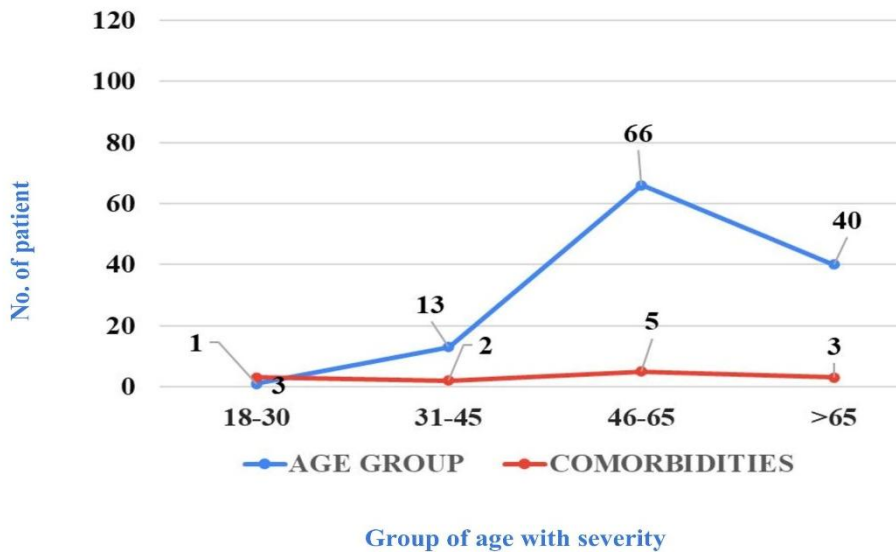
Figure 19. correlation between age and comorbidities.

Ckd is closely related to comorbidities. there is higher prevalence of multimorbidity in older age peopledue to various factors such as prolonged exposure to risk factors, biological aging processes, and cumulative effects of disease burden over time. The graph similarly represents the corelation of age and comorbidities. the no. of comorbidity (multimorbidity)is proportional to age.i.. eAverage comorbidity among people between the ages of 45 and 65 is five.

DISCUSSION

The present DUE study was conducted to determine the drug utilization pattern in chronic kidney disease.

Out of the 120 patients included, the higher incidence of CKD observed in male n=72(60%) patients due to the role of sex hormones and unhealthy lifestyle in the progression of the disease. Biological factors responsible for higher male prevalence rates include, the Damaging effects of testosterone in men. In our study, the male to female ratio was 3:2, with the male being greater than the female n=48 (40%) due to the protective effects of estrogen in women. [6]

The study determined the most affected age groups for CKD were 45–65 years, with n=66(55%), followed by the age group of more than 65 years, at n=40(33.3%). Kidney disease can develop at any time, but those over the age of 60 are more likely to develop it. The process of aging leads to a natural loss of nephrons, resulting in a decline in their effective functioning. This influences fluctuations in the estimated glomerular filtration rate (eGFR).[7]

A number of serious consequences, including an increased risk of anemia, hyperlipidemia, cardiovascular diseaseand metabolic bone abnormalities, are associated with the advancement of chronic kidney disease (CKD).In our study the two concomitant conditions with the highest prevalence were hypertension (94.16%), followed by anemia (72.5%), since the pathophysiology of CKD-associated hypertension is multifaceted and caused by several processes that gradually damage blood vessels throughout the body[8]. In our study, hypertension emerged as the predominant comorbid condition, exhibiting a direct correlation with coronary artery disease n=31(67.3%) and which is notably elevated in patients with chronic kidney disease (CKD).

Out of 120 patients, 111 were recognized as having various multimorbidity. Hypertension and diabetes-associated multimorbidity ranked highest among groups n=68(56.66 %) followed by hypertension, diabetes, and CVD-related multimorbidity n=25 (20.83%). According to Andrea Corsonello et al., CKD contributes significantly to multimorbidity in a population of older outpatients, and it is rarely observed without any co-occurring disease. The most significant co-occurring pairs involving CKD included hypertension, anemia, CHF, atrial fibrillation, myocardial infarction, hip fracture, and, to a lesser extent, hearing impairment, diabetes, and cancer. [9].

It is generally considered that the early stages of CKD are asymptomatic. In our study, the most common sign and symptom observed through our questionnaire was decreased urine output in almost n=110(91.66%) of patients. The second-most common signs and symptoms were fatigue n=89(74.16%) and decreased appetite=71 (59.16%), which are due to the progressive decline of glomerular filtration rate in chronic kidney disease patients and are associated with a significant reduction in food intake. [10]

There are several risk factors affiliated to CKD in which age, comorbidities, obesity and smoking serves the most. In our study the comorbidities n=118 (63.78%) and age n=59 (31.89%) were common factors. Two major and modifiable risk factors for kidney damage are obesity and smoking, which contribute to its pathogenesis through various mechanisms including inflammation, oxidative stress, endothelial dysfunction, prothrombotic states, hypervolemia, and adipokine imbalances, leading to conditions such as glomerulosclerosis and tubular atrophy.[11] Additionally, smoking and obesity commonly feature as shared risk factors in comorbidities associated with CKD, such as hypertension, diabetes, and cardiovascular diseases.

In our study, the majority of patients have end-stage renal disease, with n=83(69.16%) having an eGFR less than 15 ml/min because CKD commonly remains asymptomatic during the early stages, making it arduous to identify. It is worth noting that due to the paucity of symptoms, hospitalization is not necessary. This can lead to a lack of awareness of the disease, particularly among those who are in the initial stages of Stage 1 and Stage 2 CKD. With the highest prevalence rate, n = 84 patients (70%) and n = 21 patients (17.5%) are in stages G5 and G4, respectively. Dialysis makes it possible to continue living with endstage kidney disease for many years or even decades. Out of 120 patients, n=89(74.16%) individuals are on dialysis due to the majority of patients having stage G5.

Out of total utilised 1045 drugs, antihypertensive agents were the most utilised with n=221(21.41 %) as it was the highest prevalent comorbidity. According to our clinical findings in Evidence-based practice, the use of Nifedipine n=62 (71.16%) is higher than Amlodipine n=11(12.64%) due to cardio and reno protective effects it gives better patient outcomes.[12]Due to its effect on the dysregulated sympathetic nervous system and cardioprotective advantages, β-adrenoceptor antagonists, n=44(19.90 %) successfully lower blood pressure in patients with chronic kidney disease (CKD). β-blockers exhibit Reno protective properties as well, such as a decrease in the progression of interstitial fibrosis after renal damage. [13,15]

In our study, erythropoietin alfa n=57(42.85%) and iron sucrose n=38 (28.57%) is often utilized haematinics due to the high number of patients receiving haemodialysis and the higher prevalence of anemia in these individuals. According to our observations, individuals on MHD can effectively maintain their anaemic condition with 3000 IU every fifteen days along with other vitamins n=64 (31.52%) and dietary supplements=6(2.95 %).

Diuretics n=90 (52.02%)were used for the CKD patients as, therapy can reduce volume expansion and has been shown to improve left ventricular mass index and arterial stiffness in those with CKD.[14,15] sodium bicarbonate n=29(60.41 %) 500MG TDS was utilized in the patients to correct the acidosis. Febuxostat n=19(39.58 %)for decreasing the uric acid levels and providing the protective effects to kidneys.

Hyperphosphatemia stands as an independent predictor of cardiovascular disease and mortality in individuals with advanced chronic kidney disease (stages 4 and 5), attributed to impaired phosphate excretion by the kidneys.[16] In our study, calcium-based phosphate binders, notably calcium acetate (n=12, 63.15%), are prominently utilized. This choice is rooted in their efficacy in addressing the hypocalcemia often accompanying hyperphosphatemia in patients with chronic kidney disease. Additionally, non-calcium-based phosphate binders such as sevelamer (n=7, 36.84%) are also employed.

Other agents, such as K-Bind sachet n=10, (71.42%) Tolvaptan n=3(21.42%) and Potassium Chloride n=1 (7.14%) play significant roles in effectively managing electrolyte imbalances. These interventions not only address specific electrolyte deficiencies but also contribute to overall patient well-being and treatment efficacy.

Chronic administration of statins alone or in combination with aspirin has demonstrated superior short-term and long-term outcomes for in-hospital mortality when compared to both no therapy and aspirin monotherapy. This underscores the significance of utilizing combination therapies to optimize patient outcomes in the management of CVD. In our study combination cardiovascular agents, particularly formulations like aspirin + atorvastatin n=23 (54.76%), are increasingly favoured over monotherapy. This preference stems from their ability to provide primary or secondary prevention of cardiovascular disease (CVD), regardless of baseline lipid levels, particularly in patients with chronic kidney disease (CKD).[17]

In our study, a significant preference for antimicrobial monotherapy was observed, accounting for 72.22% (n=65) of cases. Notably, ceftriaxone (15.38%, n=10) and levofloxacin (15.38%, n=10) emerged as the primary choices within this category. This trend was particularly prominent among patients with end-stage renal failure, who presented with a diverse spectrum of infections including respiratory, urinary tract, and soft tissue infections, as well as meningitis and catheter-induced infections.[18] Given that diabetes is one of the prevalent comorbidities associated with chronic kidney disease (CKD), individuals are at an elevated risk of diabetic complications, including infections such as cellulitis or diabetic foot ulcers. Therefore it is necessary to provide protective antimicrobial management.

In our observational analysis, oral hypoglycemic agents DPP- 4 inhibitor n= 26 (92.85%)were highly utilized due to its renoprotective effect by reducing micro and macroalbuminuria thereby reducing the risk of ESRD in T2DM patients compared to placebo or other antidiabetic medications. [19]

Patients with progressive kidney disease face an elevated risk of hypoglycemia due to diminished insulin clearance, medication effects, and impaired renal gluconeogenesis stemming from reduced kidney mass. In our study, insulin usage predominated, accounting for 45.34% (n=39) of cases, surpassing other medication classes. Noteworthy considerations arise for hemodialysis patients prescribed short-acting insulin analogs like human actrapid. These patients necessitate dosage adjustments, with a reduction of 25% recommended when glomerular filtration rate (GFR) ranges from 10 to 50 mL/min, and a 50% reduction when GFR falls below 10 mL/min. Additionally, multiple doses of short-acting insulin should align with recommended blood sugar levels, albeit with precautions to prevent nocturnal hypoglycemia. [20]

Patients with chronic kidney disease (CKD) experience significant disruptions in bone and mineral metabolism, leading to a multifaceted disorder known as CKD-mineral bone disorder which has an elevated risk of fractures due to its intricate pathophysiology. [21]Our study findings align with this correlation, revealing a notable prevalence of calcium supplement usage, either as monotherapy n=33 (49.25 %) or in combination n=34 (50.74%). Among these, calcitriol n=21 (61.76%)and calcium + vitamin D3 n=24 (72.72%)emerged as the most frequently utilized agents.

The utilization of analgesics (n=35, 3.34%) and sedatives (n=9, 0.86%) were minimal, possibly due to the well-documented concerns associated with NSAIDs. These medications, while effective in managing pain and inflammation, can inadvertently diminish or suppress the nephroprotective functions typically associated with prostaglandins. These functions are crucial for maintaining adequate organ perfusion. Consequently, NSAIDs may induce renal ischemia, leading to azotaemia as a potential consequence.[22].

CONCLUSION

This study focuses on the utilization of drug where the antihypertensive drugs were the most utilized due to high prevalence of hypertension as comorbidity. All the drugs prescribed were with brand names. The other agents such as haematinics, diuretics, insulin, combination of cardiovascular agents and calcium supplements were recommended as per patient needs. Other agents such as antimicrobial, respiratory agents, sedatives, analgesics were prescribed to the patients based on other discordant conditions. The burden of ESRD was higher due to existing comorbidities leading to increased risk of mortality and compromised renal outcome. Furthermore, managing multimorbidity in CKD patients requires a comprehensive and multidisciplinary approach. Healthcare providers must address each condition while considering its impact on kidney function and vice versa. For example, medications used to treat one condition may interact with treatments for CKD or other comorbidities, necessitating careful monitoring and adjustment. Polypharmacy is one of the key factors which negatively impacts patient's quality of life. Therefore, it's important to conduct a periodic drug utilization study and presenting the results to the health care professionals (HCPs) to improve overall quality of drug use and for betterment of patients.

Recommended future research -The study can be conducted with consideration for multiple sites to obtain more data, analyse the data, and produce more relevant and superior results. Consanguinity and genetic inbreeding increase risk of congenital anomalies of the kidney and urinary tract and obstructive or reflux nephropathy. More attention should be given to this area. The post dialysis pain assessment and pain management can be focused on. The factors influencing the mental health of patients undergoing dialysis or having chronic conditions can be assessed. Investigation of targeted therapies that address specific molecular pathways implicated in CKD pathogenesis, such as inflammation, oxidative stress, fibrosis, and endothelial dysfunction. This includes exploring potential therapeutic targets identified through systems biology approaches.By Exploringthe use of telemedicine, mobile health apps, wearable devices, and remote monitoring technologies to facilitate CKD management, patient education, medication adherence, and timely detection of complications can be done.

ABBREVIATION

ARBs   - Angiotensin receptor blockers
BPH   **-** Benign prostatic hyperplasia
CCF   - Congestive cardiac failure
CKD   - Chronic kidney disease
COPD   - Chronic obstructive pulmonary disease
CRF   - Case report form
CVD   - Cardiovascular disease
DEC.   - Decreased
DM   - Diabetes mellitus
DUE   - Drug utilization evaluation
DVT   - Deep vein thrombosis
Egfr   - Estimated glomerular filtration rate
ESAs   - Erythropoietin stimulating agents
HD   - Haemodialysis
HTN   - Hypertension
IHD   - Ischemic heart disease
IHNI   - Inhibitors
KDIGO - Kidney disease improving global outcomes
MHD   - Maintenance haemodialysis
MVR   - Mitral valve regurgitation
SLE   - Systemic lupus erythematosus

AUTHOR'S CONTRIBUTION

The study was designed and conducted by Shraddha, Hiral, Sadiya, and Siddhraj, who also analyzed the data, interpreted the results, and drafted the manuscript. Dr. Zeel Naik and Dr. Anand Modi provided supervision of the study and critical review. The authors have given their final approval for the version to be published.

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The authors declare no conflict of interest.

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