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The Burden of Polypharmacy and Pattern of Co-Morbidities Among Chronic Kidney Disease Patients in Tertiary Care Hospital

[1]Dr. B.V. Ramana, [2]K. Supraja, [3]K.Bhavani, [4]K.Lakshmi Charitha, [5]M.Priyanka

[1]Professor, Department Of Pharmaceutics, Dr. K .V. Subba Reddy Institute Of Pharmacy,
[2,3,4,5]Pharm D Intern Students, Dr. K .V. Subba Reddy Institute Of Pharmacy

ABSTRACT

AIM

To determine the prevalence of poly-pharmacy and pattern of associated drug- drug interactions among CKD patients.

OBJECTIVE

To assess the various classes of drugs prescribed among CKD patients. To assess the drug – drug interactions. To assess the prevalence of poly-pharmacy and the pattern of associated comorbidities among CKD patients.

METHOD

A descriptive prospective study of 6 months duration that was carried out to review the medical case records of adult CKD patients attending GGH tertiary care hospital.

CONCLUSION

The prevalence of polypharmacy is predominantly high among CKD patients. The burden of polypharmacy and the pattern of associated comorbidities can result in increase in the risk of drug related problems such as drug-drug interactions, the need is to minimize the number of prescribed medications for CKD patients in order to reduce the morbidity, mortality and length of the hospital stay.

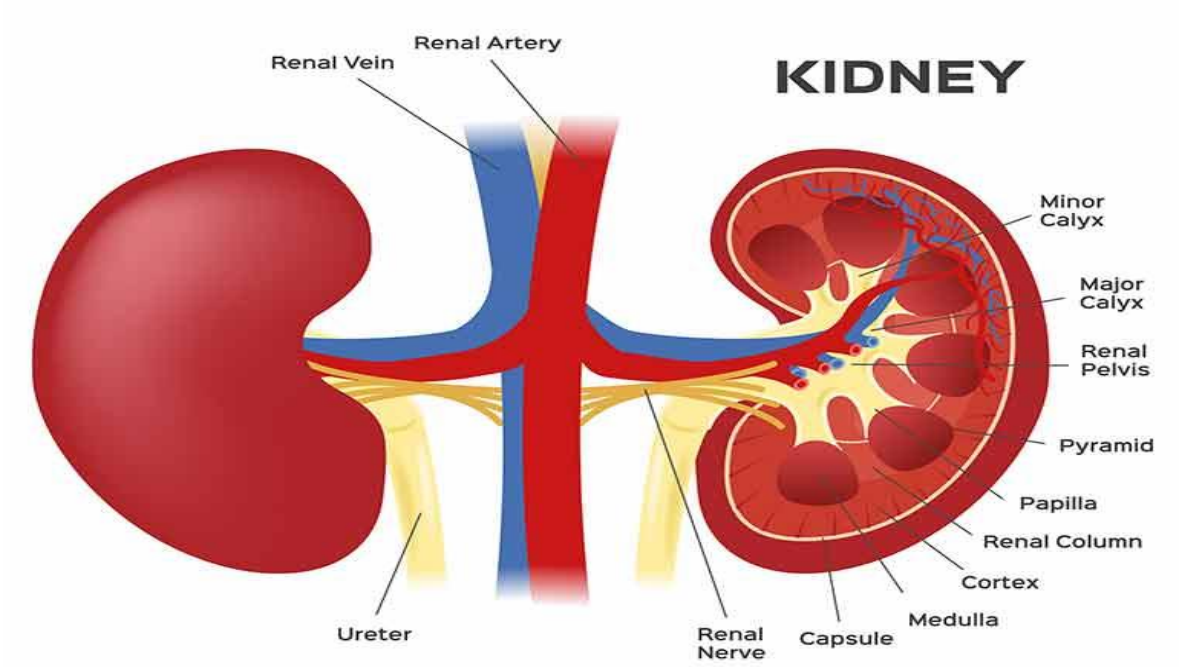
Keywords: Chronic Kidney Disease, Urinary Tract Infection, Chronic obstructive pulmonary disease

1. INTRODUCTION:

ANATOMY OF KIDNEY:

In our body kidneys are very important organs. Kidneys are bean shaped organs located on either side of the spine i.e. in the retroperitoneal space, so they are known as retroperitoneal organs. Kidneys are located between the level of last thoracic and third lumbar vertebrae protected by 11th and 12th pair of ribs. Left kidney is slightly higher than right kidney because of the presence of the liver. In Each kidney

weighs about 125 to 175 in males and 115 to 155 grams in females.It measures approximately 11 to 14 centimeters in length,6 centimeters in width and 4 centimeters thick..



Three layers of tissue surrounded by each kidney:

1. Renal capsule
2. Adipose capsule
3. Renal fascia

1.Renal Capsule:

It is a smooth, transparent, deeper layer i.e. continuous with the coat of ureter. It acts as a barrier against trauma and help in maintaining the shape of kidney.

2.Adipose Capsule:

It is a fatty tissue surrounded by renal capsule. It helps in protecting the kidney from trauma and holds in place within the abdominal cavity.

3.Renal Fascia:

It is a thin layer of dense irregular connective tissue that protects the kidney to surrounding structure and the abdominal wall. The renal fascia is deep to the peritoneum.

NEPHRON:

Nephrons are the functional units of the kidney. They produce concentrated urine by creating the ultra - filtrate. Each nephron consists of 2 main parts.

1. Renal corpuscle

2. Renal tubule

Renal corpuscles are located in renal cortex, whereas tubular system extend into medulla. Based on their distribution and morphology, there are 2 types of nephrons in the kidney

Cortical nephrons
Juxta medullary nephrons

CORTICAL NEPHRONS:
They have their corpuscles close to kidney capsule. Their tubules are very short, extending only into upper medulla.

JUXTA MEDULLARY NEPHRONS:
They are located close to cortico medullary border. Their tubular systems are much longer extending deep into medulla.

Each nephron is surrounded by group of capillaries. The branches from the renal interlobular arteries enters a nephron as **afferent arteriole**, form a capillary then exit the nephron as **efferent arteriole**. The capillaries then continues to surround the nephrons the renal tubule system as peritubular capillaries, that forms vasa recta around the nephron loop.

RENAL CORPUSCLE:
It is known as filtration apparatus of the nephron. Each corpuscle contains 2 main elements

1. GLOMERULUS
2. BOWMANS CAPSULE

The glomerulus is a network of capillaries that form the branches of the renal artery.
The bowmans capsule surrounds the glomerulus. It consists of 2 layers

1. Parietal
2. Visceral

Which bounds a cavity called glomerular capsular space. the visceral layer made up of special cells known as podocytes. Podocytes cover the wall of glomerular capillaries. The parietal layer is made up of simpe squamous epithelium and continues with the nephron tubules. The afferent and efferent arteriole enters the renal corpuscle at vascular pole, where as the site of the glomerular capsule narrows and continues as a thick segment of the nephron known as urinary pole.

The renal corpuscle is the starting point of urine formation. The systemic blood passes through glomerular capillary system and it filters to form primary urine. A special filtration barrier which selectively filters the water and solutes from the blood and passes through glomerular capillaries. The glomerular ultra-filtrate collects by glomerular space, and it passes into kidney tubules.

Kidney filtration apparatus formed by 3 layers: endothelium of the glomerular capillaries, glomerular basement membrane, podocytes. Glomerular capillaries are composed of endothelium. The glomerular basement is more complex than basal membrane.
It consists of 3 layers

1. Thick central lamina densa
2. Two thinner layers.
   a. Lamina rara interna
   b. Lamina rara externa

PODOCYTES:

It covers the wall of glomerular capillaries. Their finger like projections forms in between the projections. These 3 layers functions as selective filter, which allows the molecules below certain size, certain charge, to pass from blood and enter into renal tubular system

For example ,blood cells ,platelets ,proteins ,are prevents from leaving glomerular capillaries ,whereas water and solutes passes through .The remaining unfiltered blood is carried Out of the glomerulus by the efferent arteriole and returns to venous system.

RENAL TUBULE SYSTEM:

The tubule system which is the part of the nephron processes glomerular ultra filtrate into urine by reabsorbing necessary molecules and excretes waste substances. It contains three parts:

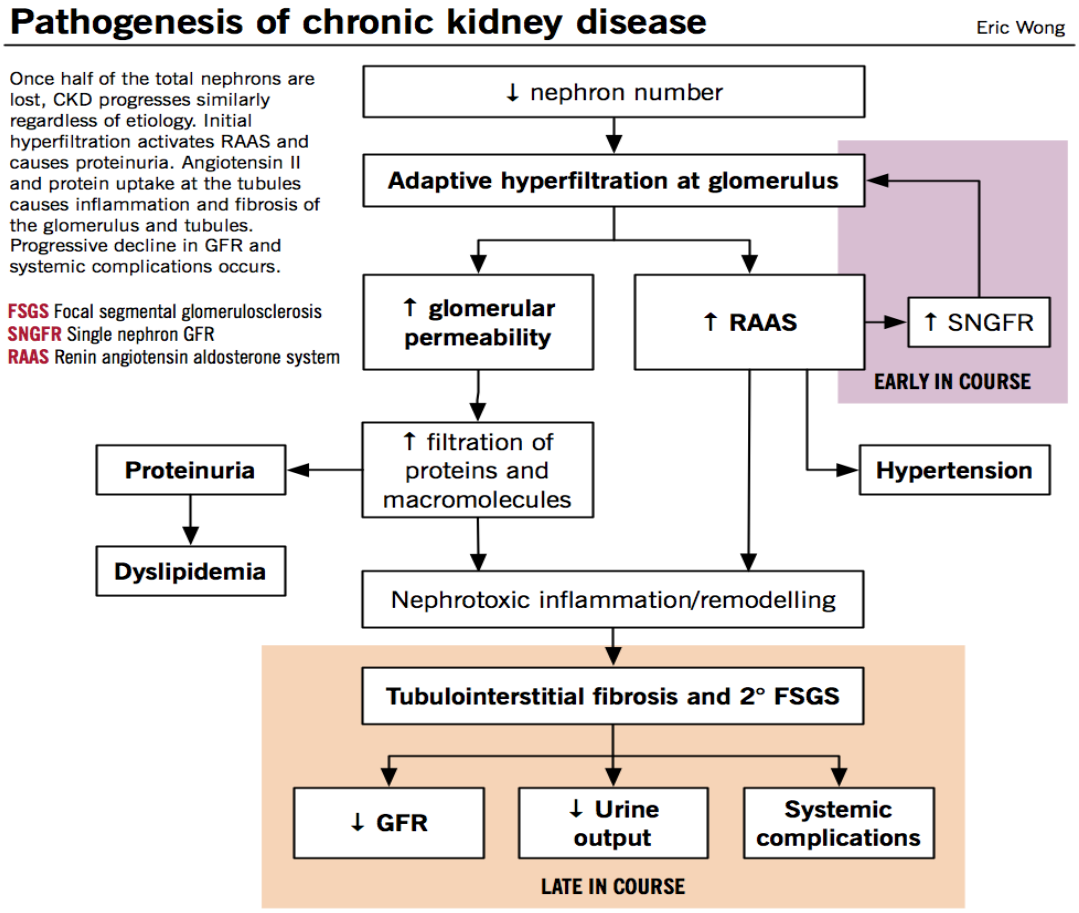
1.Proximal tubule.
2.Nephron loop.
3.Distal tubule.

PROXIMAL TUBULE:

It is the first part of the tubular system. It contains convoluted and straight segments the proximal convoluted tubule is situated in the renal cortex. The straight proximal tubule is extended into medulla these two parts are composed of simple cuboidal epithelium that are rich in mitochondria and microvilli. Half of the previously filtered water and molecules returns to the blood by the proximal tubule.

NEPHRON LOOP:

It is the U shaped structure of the nephron extending throughout the medulla of the kidney. It consists of two parts; Thin ascending and thin descending loops which are composed of simple squamous epithelium. These cells have few organelles. These two loops work with the surrounding vasa recta capillaries to adjust the salts like sodium, chloride, potassium and water levels. The descending limb is more permeable to water while the ascending limb is more permeable to solutes.



2. AIMS AND OBJECTIVES

AIM:

To determine the prevalence of poly-pharmacy and pattern of associated drug- drug interactions among CKD patients**.**

OBJECTIVES:

To assess the various classes of drugs prescribed among CKD patients. To assess the drug – drug interactions. To assess the prevalence of poly-pharmacy and the pattern of associated comorbidities among CKD patients.

3. METHODOLOGY

STUDY DESIGN:

A descriptive prospective study

STUDY DURATION:

The present study was carried out for a period of 6 months.

STUDY SITE:

Nephrology department, Inpatient unit of Government General Hospital , Kurnool.

SAMPLE SIZE:

During the study of six months, the total of 150 cases was collected and studied.

SOURCE OF DATA:

- All the patients satisfying the inclusion criteria were selected from a nephrology department in Government General Hospital, Kurnool.
- All the required data was collected from patients through personal interview and case sheets.

Inclusion criteria:

- Patients with CKD both male and female .
- Patients above 18 years are included.
- Patients with co-morbid conditions like hypertension ,diabetes ,CAD, Obesity ,CVA, Anaemia, old PTB, Asthma, Hypothyroidism.

Exclusion criteria:

- Patients below 18 years are excluded
- Pregnant patients are excluded.
- Psychiatry patients are excluded.
- Patients with critical illness are excluded.

METHOD OF COLLECTION OF DATA:

- All the patients were satisfying the inclusion criteria were selected from the nephrology department in Government General Hospital, Kurnool.
- All the data of the subject are collected by using the proforma
- The data collection includes Demographic details, History of present illness, Treatment history, Past psychiatric/medication history, Family history, Personal history and allergies, Laboratory investigations, Diagnosis, Drug chart.

SATISTICAL ANALYSIS:

- This is a descriptive prospective study carried out at the nephrology department in a tertiary care hospital in Kurnool.
- Chi square test were used to compare means and proportions respectively
- The level of significance was set at $p< 0.05$

4. RESULTS:

The study involved 100 consented CKD patients comprising 67males and 33females. (p value =0.21)

Gender	**<30**	**31-40**	**41-50**	**51-60**	**61-70**	**>71**	**MEAN AGE**
Male	6	10	20	21	10	-	13.4%

Female	5	5	8	5	9	1	5.5%
Total	11	15	28	26	19	1	16.7%

Tab 1: Gender distribution

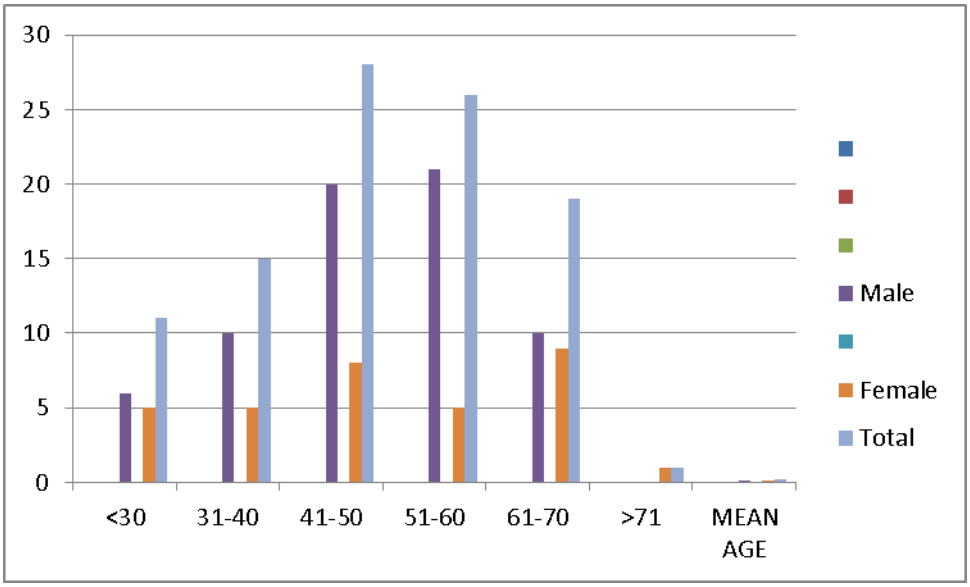


Fig. 1. Gender distribution

The most common comorbidities:

COMORBIDITIES	MALES	FEMALES	TOTAL	Prevalence
HYPERTENSION + ANAEMIA	34	22	56	56%
HTN + DM	5	0	5	5%
HTN + DM + CAD	1	0	1	1%
HTN + DM + ANAEMIA	11	2	13	13%
HTN + HYPOTHYROIDISM + ANAEMIA + DM	0	1	1	1%
HTN + ANAEMIA + CAD	1	0	1	1%
CAD + ANAEMIA	3	0	3	3%
HTN + ANAEMIA + HYPOTHYROIDISM	0	3	3	3%
DM + Anaemia	3	1	4	4%
ANAEMIA	5	0	5	5%
Old PTB + ANAEMIA	1	1	2	2%
HTN + COPD + ANAEMIA	2	0	2	2%

HTN + CAD + ANAEMIA	1	0	1	1%
CAD	1	0	1	1%
HTN + Old PTB + ANAEMIA	1	0	1	1%

Table 2: Comorbidities among chronic kidney disease.

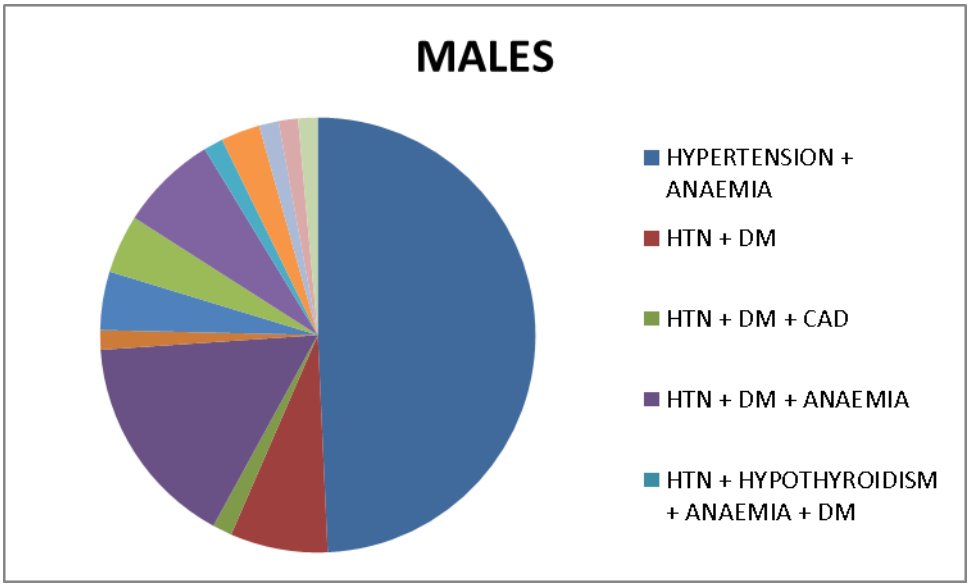


Fig.2. Comorbidities among chronic kidney disease.

- Most proportion of the respondents 70 had two comorbidities, followed by 23 with three comorbidities, 6 with one comorbidity.
- The highest comorbidity prevalence rate was seen in HTN + ANAEMIA -56% HTN + ANAEMIA + DM – 13%, HTN +DM – 5%, ANAEMIA -5%, DM + ANAMEIA – 4%, HTN + ANAMEIA + HYPOTHYROIDISM – 3% (p value – 0.08)

The most frequently prescribed Classes of drugs:

DRUGS	**<30**	**31-40**	**41-50**	**51-60**	**61-70**	**>71**	**TOTAL**
ANTIBIOTICS:							
.PIPERACILLIN +TAZOBACTUM.	**2**	**2**	**5**	**7**	**2**	**-**	**18**
AZITHROMYCIN				**1**			**1**
.CEFTRIAXONE		**3**	**12**	**10**	**3**		**28**
METRONIDAZOLE		**1**	**1**	**1**	**4**		**7**
AMOXICILLIN		**1**	**5**	**2**	**2**		**10**
CEFIXIME	**3**	**3**	**2**	**2**			**10**
CEFOPERAZONE+SULBACTAM	**1**	**1**	**3**	**5**	**6**		**16**
CLINDAMYCIN					**1**		**1**

ALKALIZING AGENT:							
SODIUM BICARBONATE	**4**	**9**	**18**	**19**	**8**		**58**
ANTI-HYPERTENSIVES:							
AMLODIPINE	**6**	**6**	**18**	**16**	**7**		**53**
.FUROSEMIDE		**4**	**15**	**15**	**5**		**44**
METOPROLOL	**3**	**6**	**13**	**11**	**2**		**35**
CLONIDINE	**2**	**4**	**5**	**1**			**12**
.PRAZOSIN							
.LABETALOL		**1**					**1**
NIFEDIPINE							
TELMISARTAN		**1**					**1**
NICARDIPINE		**2**	**1**	**1**			**4**
HYPOGLYCEMICS							
METFORMIN			**1**				**1**
GLIMIPERIDE			**1**				**1**
HUMULIN -R			**1**				**1**
NOVOLOG-R			**1**				**1**
H.ACTRAPID			**4**	**5**	**1**		**10**
MIXTARD					**1**		**1**
H2 RECEPTOR BLOCKERS							
RANTAC	**6**	**5**	**18**	**18**			**47**
VITAMIN SUPPLEMENTS							
TAB.B COMPLEX	**6**	**10**	**20**	**21**	**10**		**67**
TAB.Ca+2+VIT D3	**6**	**10**	**20**	**21**	**10**		**67**
TAB.IRONFOLIC ACID	**6**	**10**	**20**	**21**	**10**		**67**
CALCIUM SALTS							
CALCIUM GLUCONATE		**2**	**11**	**6**	**4**		**23**
ANTI- EMETICS							
ONDANSETRON		**2**	**3**	**6**	**2**		**13**
OTHER DRUGS							
SYP.AMBROXYL HYDRCHLORIDE							
MANNITOL		**2**					**2**
ATORVASTATIN		**4**	**2**		**1**		**7**
ASPIRIN		**2**	**1**	**7**	**1**		**11**
CYCLOPAM							
SPOROLAC		**1**					**1**
PARACETAMOL		**2**	**5**	**6**	**2**		**15**
FEBUXOSTAT		**1**					**1**

Tab.3- IN MALES-The most frequently prescribed Classes of drugs

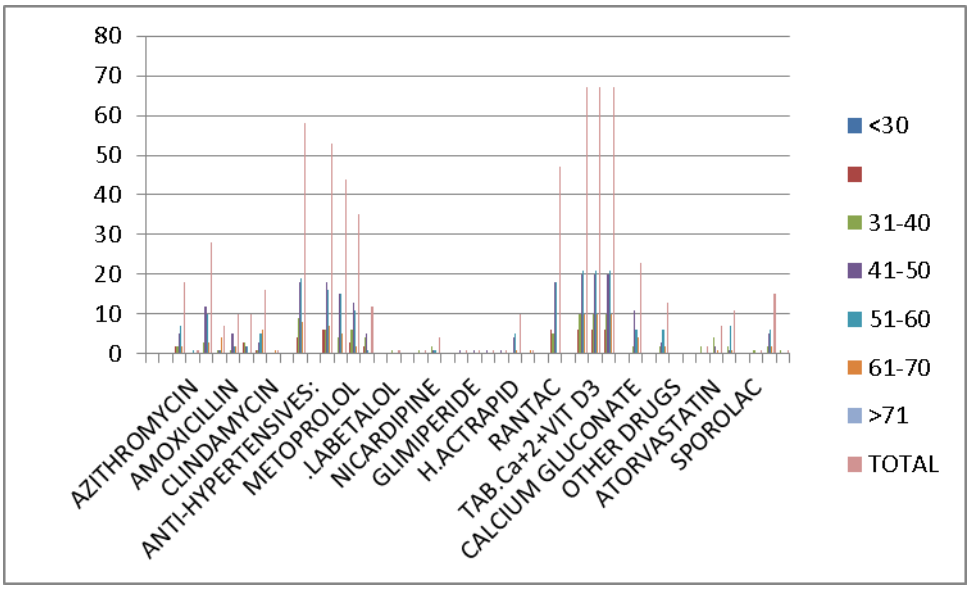


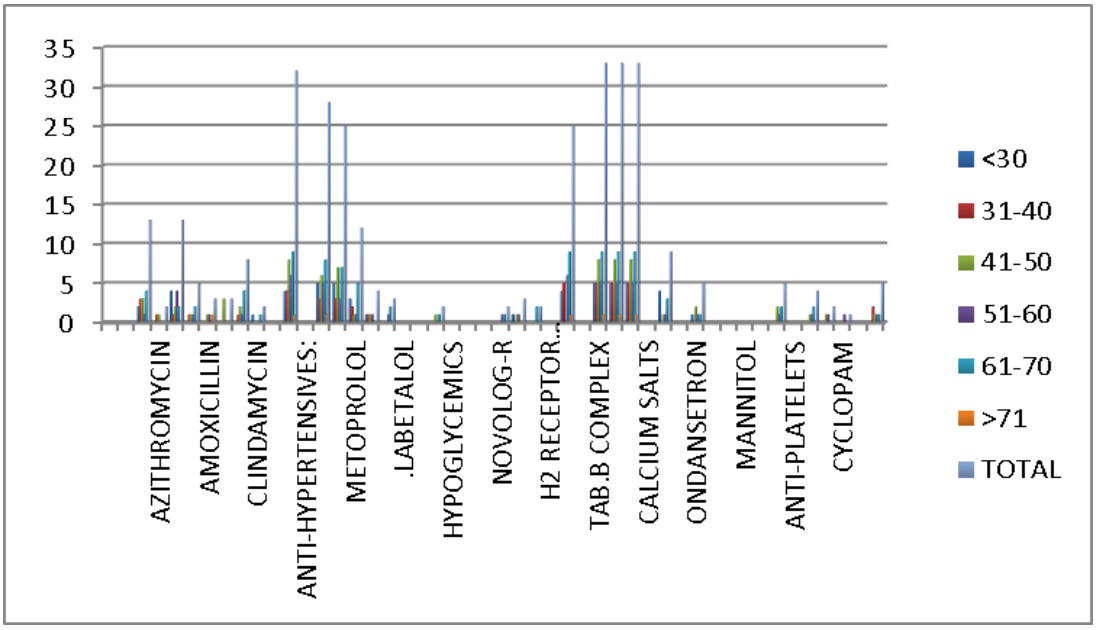
Fig.3- IN MALES-The most frequently prescribed Classes of drugs

- IN FEMALES-

DRUGS	<30	31-40	41-50	51-60	61-70	>71	TOTAL
ANTIBIOTICS:							
.PIPERACILLIN +TAZOBACTUM.	2	3	3	1	4		13
AZITHROMYCIN		1	1				2
.CEFTRIAXONE	4	1	2	4	2		13
METRONIDAZOLE		1	1	1	2		5
AMOXICILLIN			1	1		1	3
CEFIXIME			3				3
CEFOPERAZONE+SULBACTAM		1	2	1	4		8
CLINDAMYCIN	1				1		2
ALKALIZING AGENT:							
TAB.SODIUM BICARBONATE	4	4	8	6	9	1	32
ANTI-HYPERTENSIVES:							
AMLODIPINE	5	3	6	5	8	1	28
.FUROSEMIDE	5	3	7	3	7		25
METOPROLOL	3	2	1	1	5		12
CLONIDINE	1	1	1	1			4
.PRAZOSIN				1	2		3
.LABETALOL							
NIFEDIPINE							
NICARDIPINE			1		1		2

HYPOGLYCEMICS							
METFORMIN							
HUMULIN -R							
NOVOLOG-R				**1**	**1**		**2**
H.ACTRAPID	**1**		**1**	**1**			**3**
MIXTARD					**2**		**2**
H2 RECEPTOR BLOCKERS							
RANTAC	**4**	**5**		**6**	**9**	**1**	**25**
VITAMIN SUPPLEMENTS							
TAB.B COMPLEX	**5**	**5**	**8**	**5**	**9**	**1**	**33**
TAB.Ca+2+VIT D3	**5**	**5**	**8**	**5**	**9**	**1**	**33**
TAB.IRONFOLIC ACID	**5**	**5**	**8**	**5**	**9**	**1**	**33**
CALCIUM SALTS							
CALCIUM GLUCONATE	**4**		**1**	**1**	**3**		**9**
ANTI- EMETICS							
ONDANSETRON	**1**		**2**	**1**	**1**		**5**
OTHER DRUGS							
SYP.AMBROXYL HYDRCHLORIDE							
MANNITOL							
STATIN							
ATORVASTATIN			**2**	**1**	**2**		**5**
ANTI-PLATELETS							
ASPIRIN			**1**	**1**	**2**		**4**
FEBUXOSTAT			**1**	**1**			**2**
CYCLOPAM				**1**			**1**
SPOROLAC							
PARACETAMOL		**2**	**1**	**1**	**1**		**5**

Tab.4. IN FEMLAES-The most frequently prescribed Classes of drugs



Tab.4. IN FEMLAES-The most frequently prescribed Classes of drugs

• A 68 ckd patients were on 6-10 medications, 30 were on 11-15 medications and 2 were on > 16 medications.

In this study, poly-pharmacy (the concurrent use of more than 5 different medications by a patient) was observed among 100 CKD patients

• Among these CKD patients the prevalence of poly-pharmacy was 100%.

DRUG – DRUG INTERACTIONS were found in 45cases of 100 CKD patients.

- **POTENTIAL DRUGS INTERACTIONS ACCORDING TO GENDER:**

Gender	<30	31-40	41-50	51-60	61-70	>71	MEAN AGE
Male	3	5	10	10	6	-	**6.8%**
Female	1	2	3	1	4	-	**2.2%**
Total	4	7	13	11	10	-	**9.0%**

Tab.5. POTENTIAL DRUGS INTERACTIONS ACCORDING TO GENDER

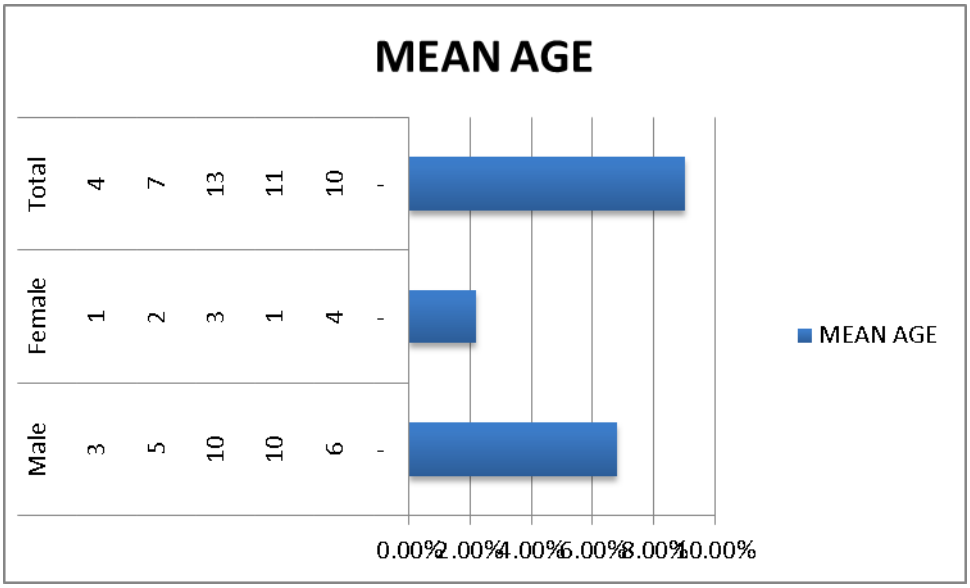


Fig.5. POTENTIAL DRUGS INTERACTIONS ACCORDING TO GENDER

- Total drug – drug interactions were 72

- **POTENTIAL MAJOR INTERACTIONS WERE:**

S.NO.	DRUG –DRUG INTERACTIONS	EFFECTS
1.	CLONIDINE + METOPROLOL	Increased risk of sinus bradycardia, Acute hypertension (withdrawal response)
2.	ACETAMINOPHEN/TRAMADOL HCL + RANITIDINE HCL	Increased risk of respiratory depression
3.	ASPIRIN + FUROSEMIDE	Reduced furosemide effectiveness & possible nephrotoxicity
4.	ASPIRIN + CLOPIDOGREL	Increased risk of bleeding
5.	AMIODARONE + RANITIDINE	Increased amiodarone exposure
6.	AMOXICILLIN+DOXYCYCLINE	Decreased amoxicillin effectiveness
7.	METRONIDAZOLE + ONDANSETRON	Increased risk of QT- interval prolongation and arrhythmias
8.	ALPRAZOLAM + RANITIDINE	Increased alprazolam exposure
9.	AZITHROMYCIN + METRONIDAZOLE	Increased risk of QT interval and arrhythmia

Tab.5 MAJOR Drug interactions among CKD.

MODERATE INTERACTIONS WERE:

S.NO.	DRUG – DRUG INTERACTIONS	EFFECTS
1.	ASPIRIN + METOPROLOL	Increased blood pressure
2.	ASPIRIN + SODIUM BICARBONATE	Decreased salicylate effectiveness
3.	ASPIRIN + CALCIUM GLUCONATE	Decreased salicylate effectiveness
4.	METOPROLOL + PRAZOSIN	Exaggerated hypotensive response to 1st dose of prazosin
5.	CALCIUM GLUCONATE + DOXYCYCLINE	Decreased effectiveness of doxycycline
6.	AMIODARONE + TORSEMIDE	Increased plasma levels of torsemide
7.	CALCIUM GLUCONATE + CEFTRIAXONE	May result in precipitation
8.	FUROSEMIDE + HYDROCORTISONE	Hypokalemia

Tab.6. MODERATE INTERACTIONS Drug interactions

MINOR INTERACTIONS WERE:

S.NO.	DRUG – DRUG INTERACTIONS	EFFECTS
1.	ASPIRIN + RANITIDINE	Reduced plasma levels and decreased antiplatelet effect of aspirin
2.	FERROUS SULFATE + SODIUM BICARBONATE	Decreased Iron effectiveness

Tab.7. MINOR INTERACTIONS Drug interactions

DRUG – DRUG INTERACTION SEVERITY IN MALES;

SEVERITY	<30	31-40	41-50	51-60	61-70	>71	TOTAL	Mean
MAJOR	2	5	11	10	4	-	32	6.4%
MODERATE	1	4	4	6	2	-	17	3.4%
MINOR	1	-	-	1	1	-	3	1%

Table.8. Drug interactions in male patients.

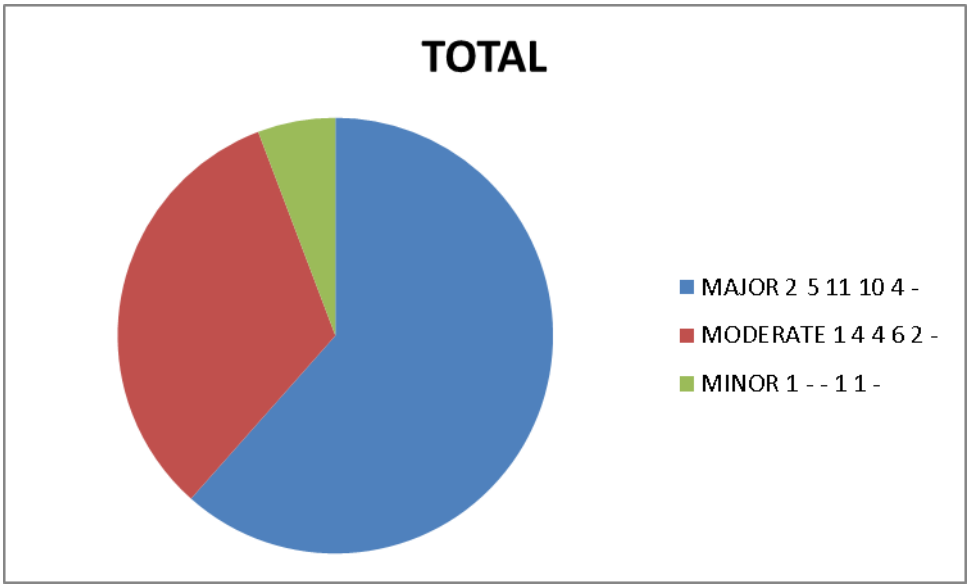


Fig.6. Drug interactions in male patients.

DRUG-DRUG INTERACTION SEVERITY IN FEMALES:

SEVERITY	<30	31-40	41-50	51-60	61-70	>71	TOTAL	MEAN
MAJOR	1	2	2	2	3	-	11	2.0%
MODERATE	-	-	4	1	4	-	9	3%
MINOR	-	-	-	-	-	-	0	0%

Tab.9 Severity of drug interactions in females.

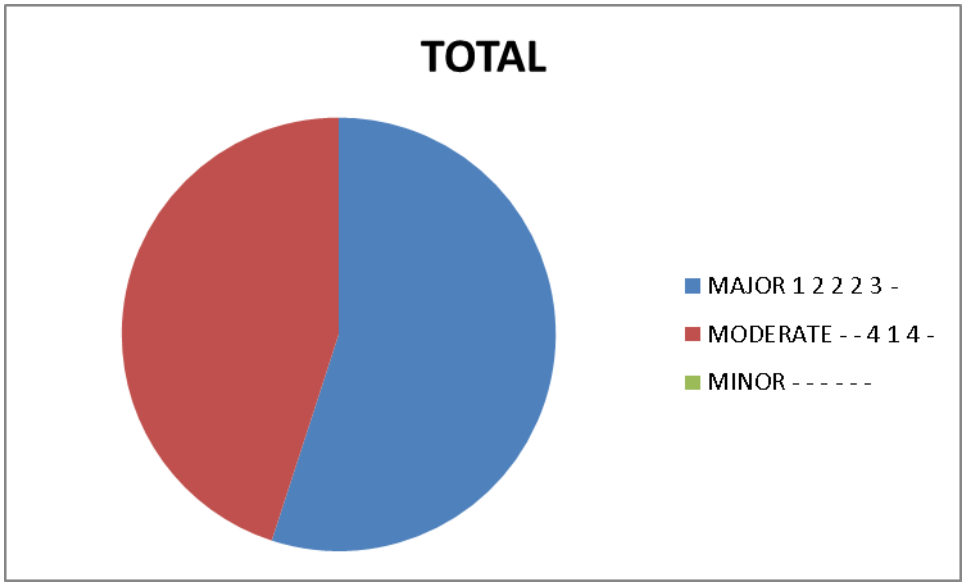


Fig.7. Severity of drug interactions in females

OBSERVED DRUG – DRUG INTERACTIONS:

S.NO	DRUG – DRUG INTERACTIONS	EFFECT	EVIDENCE
1	CLONIDINE + METOPROLOL	Increased risk of sinus bradycardia	DAY 1 – 120bpm Therapy started -DAY 2 – 100bpm DAY3 – 90bpm DAY4 – 83bpm Day5 – 79bpm Day6 – 72bpm
2	METOPROLOL + PRAZOSIN	Exaggerated rate of hypotensive responsive to first dose of alpha blocker	Day1-170/90 mm of Hg Day2 -160/80 mm of Hg Started therapy - Day3-100/60 mm of Hg Day 4 -90/70 mm of Hg Day5 – 90/60 mm of Hg
3	ASPIRIN + FUROSEMIDE	Reduced furosemide effectiveness	Decreased urine output – 100ml
4	ASPIRIN + METOPROLOL	Increased blood pressure	Day1 – 170/120mm of Hg Day2- 160/110 mm of Hg Therapy started - Day3- 180/100 mm of Hg Day4 – 190/100 mm of Hg Day 5 – 180/110 mm of Hg

Tab.10. OBSERVED DRUG – DRUG INTERACTIONS

5. DISCUSSION

Our prospective observational study was carried in nephrology department among 100 CKD patients. The majority of CKD patients were males, this shows that CKD is more predominant among males because of life style changes such as chronic smoking, chronic alcohol consumption, poor nutritional habits, inadequate exercise, stress. The mean age of the males 13.4% and females were 5.5%. (p value = 0.21)

The practice of polypharmacy in the management of CKD is however more because it contains high number of comorbidities and some complications such as Hypertension, diabetes mellitus , coronary artery disease , anaemia, COPD, cerebro vascular accident, hypothyroidism, old PTB, can be managed by combination of the drugs.

The study shows 100 patients were on polypharmacy i.e. concurrent use of more than 5 different medications. The most common comorbidities in the study were Hypertension, diabetes, anaemia. (p value =0.08)

In our study, the prevalence rate of polypharmacy among CKD patients were 100%. This reveals that out of 100 patients are diagnosed as CKD recruited in the study having prescribed more than 5 different medications for every visit of the tertiary care hospital. Depending on the need for a physician and clinical pharmacist to evaluate the prescription of CKD patients for a possible drug related problems.

In our study, the concurrent use of more than 5 different medications per prescription and number of different comorbidities per patient was found to be major. This shows that prevalence rate for polypharmacy is more among CKD patients.

The most frequently prescribed medications in the study were vitamin supplements, sodium bicarbonate, amlodipine, ranitidine, furosemide, metoprolol, ceftriaxone, calcium gluconate, piperacillin + tazobactum, cefoperazone + sulbactum, paracetamol, ondansetron, aspirin, atorvastatin. A total number of 72 potential drug – drug interactions were observed among 100 patients and the most frequent drug interaction was between clonidine and metoprolol. our study shows that CKD patients with different comorbidities can have raise in the prescribed medications i.e. polypharmacy

The prevalence of polypharmacy was found to be increased because of number of medications per prescription, number of associated comorbidities, increasing age, increase in serum creatinine levels, and some common comorbidities such as hypertension, diabetes, anaemia were the risk factors associated with CKD patients to poly-pharmacy. Our study provides the magnitude and burden of polypharmacy associated comorbidities among CKD patients and helps to prevent the occurrence of drug related problems such as drug – drug interactions.

6. CONCLUSION

The prevalence of poly-pharmacy is predominantly high among CKD patients. The burden of poly-pharmacy and the pattern of associated comorbidities can result in increase in the risk of drug related

problems such as drug-drug interactions, the need is to minimize the number of prescribed medications for CKD patients in order to reduce the morbidity, mortality and length of the hospital stay.In our study the number of medications per prescription and number of associated comorbidities per patient were found to be the major determinants of prevalence rate for polypharmacy among CKD patients. The clinical pharmacist should regularly monitor and review the prescription of CKD patients to prevent drug related problems such as drug-drug interactions.

7. Reference

1. AbuRuz SM, Alrashdan Y, Jarab A, Jaber D, Alawwa IA. Evaluation of the impact of pharmaceutical care service on hospitalized patients with chronic kidney disease in Jordan. International journal of clinical pharmacy. 2013 Oct;35:780-9.
2. Aggarwal HK, Jain D, Meel S. Impact of patient education and knowledge on medication adherence in chronic kidney disease patients. Journal, Indian Academy of Clinical Medicine. 2018 Jul;19(3):166-74.
3. Zhang QL, Rothenbacher D. Prevalence of chronic kidney disease in population-based studies: systematic review. BMC public health. 2008 Dec;8(1):1-3.
4. Khan UA, Garg AX, Parikh CR, Coca SG. Prevention of chronic kidney disease and subsequent effect on mortality: a systematic review and meta-analysis. PLoS One. 2013 Aug 29;8(8):e71784.
5. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. New England Journal of Medicine. 2004 Sep 23;351(13):1296-305.
6. Titze S, Schmid M, Köttgen A, Busch M, Floege J, Wanner C, Kronenberg F, Eckardt KU, GCKD Study Investigators, Eckardt KU, Titze S. Disease burden and risk profile in referred patients with moderate chronic kidney disease: composition of the German Chronic Kidney Disease (GCKD) cohort. Nephrology Dialysis Transplantation. 2015 Mar 1;30(3):441-51.
7. Adibe MO, Ewelum PC, Amorha KC. Evaluation of drug-drug interactions among patients with chronic kidney disease in a South-Eastern Nigeria tertiary hospital: a retrospective study. Pan African Medical Journal. 2017;28(1).
8. Ajimura CM, Jagan N, Morrow LE, Malesker MA. Drug interactions with oral inhaled medications. Journal of Pharmacy Technology. 2018 Dec;34(6):273-80.
9. Al Raiisi F, Stewart D, Fernandez-Llimos F, Salgado TM, Mohamed MF, Cunningham S. Clinical pharmacy practice in the care of Chronic Kidney Disease patients: a systematic review. International journal of clinical pharmacy. 2019 Jun 15;41:630-66.
10. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, Saran R, Wang AY, Yang CW. Chronic kidney disease: global dimension and perspectives. The Lancet. 2013 Jul 20;382(9888):260-72.
11. Herzog CA, Asinger RW, Berger AK, Charytan DM, Díez J, Hart RG, Eckardt KU, Kasiske BL, McCullough PA, Passman RS, DeLoach SS. Cardiovascular disease in chronic kidney disease. A clinical update from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney international. 2011 Sep 2;80(6):572-86.
12. Di Angelantonio E, Chowdhury R, Sarwar N, Aspelund T, Danesh J, Gudnason V. Chronic kidney disease and risk of major cardiovascular disease and non-vascular mortality: prospective population based cohort study. Bmj. 2010 Sep 30;341.

13. Borné Y, Nilsson PM, Melander O, Hedblad B, Engström G. Multiple anthropometric measures in relation to incidence of diabetes: a Swedish population-based cohort study. The European Journal of Public Health. 2015 Dec 1;25(6):1100-5.
14. Bajait CS, Pimpalkhute SA, Sontakke SD, Jaiswal KM, Dawri AV. Prescribing pattern of medicines in chronic kidney disease with emphasis on phosphate binders. Indian journal of pharmacology. 2014 Jan;46(1):35.
15. Singh AK, Farag YM, Mittal BV, Subramanian KK, Reddy SR, Acharya VN, Almeida AF, Channakeshavamurthy A, Ballal HS, Issacs R, Jasuja S. Epidemiology and risk factors of chronic kidney disease in India–results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. BMC nephrology. 2013 Dec;14(1):1-0.