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EVALUATION OF PATIENT COMPLIANCE AND DEPRESSIVE SYMPTOMS ASSOCIATED WITH POLYPHARMACY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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ABSTRACT

Background: CKD is defined as an irreversible condition with abnormalities of kidney structure or function, present for > 3months, with implication of health. Kidney damage includes a wide range of abnormalities and is observed during clinical assessment. GFR is accepted as the overall index of kidney function. It is very difficult to identify CKD in its early stage. Several issues contribute to high prevalence in India. Diabetes and hypertension account for 40%-60% CKD in India. As per Indian Counsel of Medical Research, prevalence of CKD is increased by 6.3%. Due to lifestyle diseases there is a 30% increase in the CKD in US. Smoking, obesity, older age family history also contributes to the development of CKD. In our study male patients with older age are dominant with CKD. **Objectives:** The main objectives was to assess the compliance and depressive symptoms among the patients receiving polypharmacy in Chronic Kidney Disease. **Materials And Methods:** Prospective observational analysis of CKD cases admitted to KR Hospital over a period of 6 months from November 2018 to April 2019 was carried out with a sample size of 168. The data obtained was analyzed by using SPSS version 20. **Result:** Among 168 patients 111 patients were male patients and 57 patients were females. In the study population 77 patients were low adherent to the treatment and 60 patients were moderately adherent and 31 patients were highly adherent. In 168 patients 56 patients were with minimal depressive symptoms (33.3%), 57 patients were with mild depressive symptoms (33.9) and 36 patients with moderate depressive symptoms (21.4%). Only 4 patients were observed with severe depression (2.4%). In the study furosemide was the drug that caused highest incidence of ADR. Conclusion: Our study reveals that most of the patients are with poor adherence to medication. Depressive symptoms are more prevalent in CKD patient. Most of the patients in our study were shown minimal depressive symptoms and incidence of depression was more observed in female patients. In CKD patients depression is unrecognizable in most of the patients. So it is the duty of the pharmacist to make aware the patients about the indication and side effect of the drugs. And also to provide patient counseling to make the society to more adherent to the medication and to prevent depression.

KEYWORDS: Chronic Kidney Disease (CKD), Patient compliance, Depressive symptoms, polypharmacy, Adverse Drug Reaction.

INTRODUCTION

Chronic Kidney Disease is a progressive loss in renal function over a period of months or years and a devastating medical, social and economic problem for patients and their families. Chronic Kidney Disease is a major problem which requires concurrent use of several medications. Kidney diseases itself don't need the use of medications in most cases. But, co- morbidities associated with Chronic Kidney Disease like hypertension and Diabetic Mellitus require use of several drugs. Hence polypharmacy in Chronic Kidney Disease is unavoidable.[1]

Medication adherence rates are diminished by complex drug regimens, incomplete explanation of benefits and side effects, cost of medications etc. Generally polypharmacy will create problems include chances of poor adherence and ADRs. Moreover in CKD, the functioning of kidney is poor and causes decrease elimination of drugs, may leads to serious consequences.[2]

In patients with ESRD there are many causes of depression. The prognosis of the depression is considerably higher in patients with CKD than in general population. Kidney patients and their families experience losses associated with health loss, loss of independence, loss of active contribution at home, loss of privileges of patient and all that resulted in social role, economic

wealth losses and emotional losses.

MATERIALS AND METHODOLOGY

The study will be conducted in the department of Neurology, Krishna Rajendra hospital, Mysore. Krishna Rajendra Hospital (K R- Hospital) and Cheluvamba Hospitals are both Tertiary Referral Centers and Teaching Hospitals attached to the Mysore Medical College. The study duration was from Ethical approval was obtained from the institutional ethical committee of Mysore medical college and research institute and associated hospital, Mysuru.

A specially designed data collection form was devised for the study. All relevant data of the enrolled patients including demographic details; clinical data such as diagnosis, laboratory data, past medical history, past medication history, comorbidities; therapeutic data such as drug name, dose, frequency, route and duration of administration was collected from various data sources. The same details were documented electronically in specially designed database. Clinical data and detailed regarding drug usage and laboratory data were collected from clinical case record and entered into the proforma. The same were numerically coded and entered into SPSS version 20. The data have been summarised by routine descriptive statistics namely mean and standard deviation for numeric variables and counts and percentage for categorical variables.

All patients meeting the study criteria was enrolled in the study after obtaining the informed consent. All enrolled patients was followed up at nephrology department each day till treatment completed. Patient selected were above 18 years of age.

To assess the medication adherence Morisky Green Levine Medication Adherence Scale was used. To determine the causality of ADR's by Naranjo Algorithm and to assess the severity of ADR's by Hart Wig severity assessment scale. Patient Health Questionnaire-9 (PHA-9) was used for the evaluation of the severity of the depression.
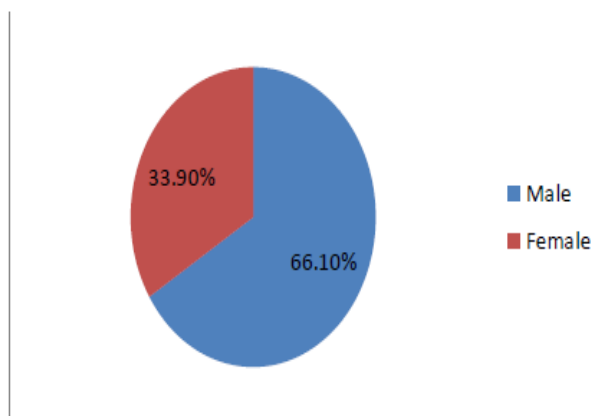
Result

Figure: 1 Gender Distribution.

Table 1: Age Distribution.

Age group	Number of Patients	Percentage
<20 Years	6	3.5
20-30 Years	15	8.9
31-50 Years	53	31.5
51-65 Years	58	34.5
>65Years	36	21.4

Table 2: Educational Categorization.

Education	No of patients	Percent
Illiterate	46	27.4
Primary	83	49.4
Secondary	35	20.8
Tertiary	4	2.4
Total	168	100

Table 3: Duration of the CKD.

Duration	No of Patients	Percentage
<1 Year	35	20.83
1-3 Years	123	73.2
3-5 Years	10	5.95
TOTAL	168	100

Table: 4 Number of the drugs used.

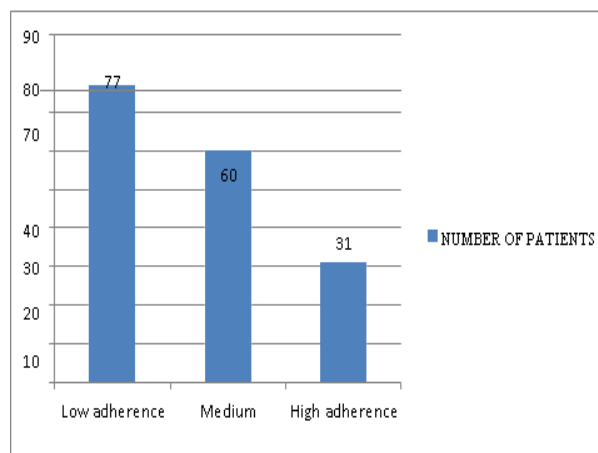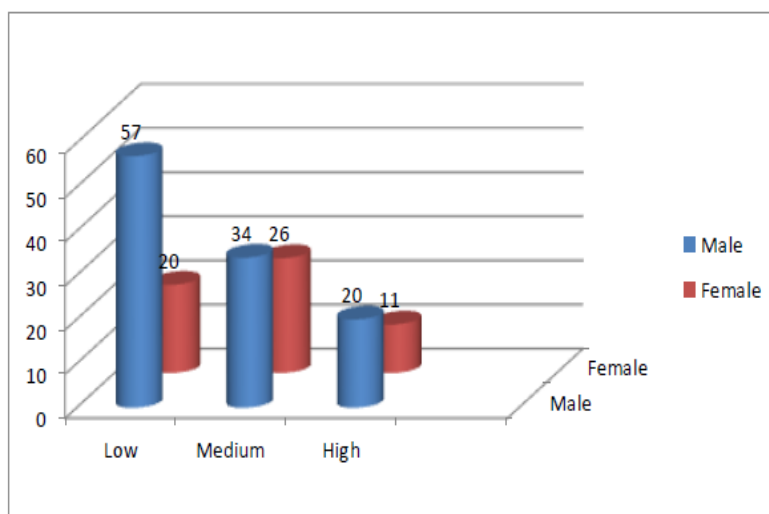| Drugs	Number of Patients	Percentage
5-7 Drugs	38	22.6
8-9 Drugs	91	56.2
10-11 Drugs	28	16.7
>10 Drugs	11	6.5
Total	168	100

Figure 2: Medication Adherence in the study population.

Table 5: Association Of Medication Adherence with Age Group.

Medication Adherence	Age Group	Number Of patients	Percentage
Low adherence	<20 years 20-30 years 31-50 years 51-65 years >65 years Total	2 4 13 44 14 77	2.6 5.2 16.9 57.1 18.2 100
Medium adherence	<20 years 20-30 years 31-50 years 51-65 years >65 years Total	1 4 24 12 19 60	1.7 6.7 40 20 31.7 100
High adherence	<20 years 20-30 years 31-50 years 51-65 years	3 7 16 2	9.7 22.6 51.6 6.5
	>65 years Total	3 31	9.6 100

Figure 3: Association of Medication Adherence with Gender.

Table 6: Depressive Symptoms in Study Population.

Depressive Symptoms	Number of Patients	Percent
Minimal depression	56	33.3
Mild depression	57	33.9
Moderate depression	36	21.4
Moderately severe depression	15	8.9
Severe depression	4	2.4
Total	168	100

Table: 7Association of Depressive Symptoms with Age.

Depressive symptoms	Patient's age group	No of patients	Percentage
Minimal depression	<20 years 20-30 years	1 6	1.8 10.7

	31-50years	24	42.9
	51-65years	18	32.14
	>65years	7	12.5
	Total	56	100
Mild depression	<20 years	2	3.5
	20-30 years	7	12.3
	31-50years	19	33.3
	51-65years	27	47.7
	>65years	2	3.5
	Total	57	100
Moderate	<20 years	2	5.6
	20-30 years	2	5.6
	31-50 years	2	5.6
	51-65 years	9	25
	>65 years Total	21	58.3
		36	100
Moderately severe	31-50 years	5	33.3
	51-65 years	4	26.7
	> 65years	6	40.0
	Total	15	100
Severe	<20 years	1	25
	31-50 years	3	75
	Total	4	100

Table: 8 Association of Depressive Symptoms with Age.

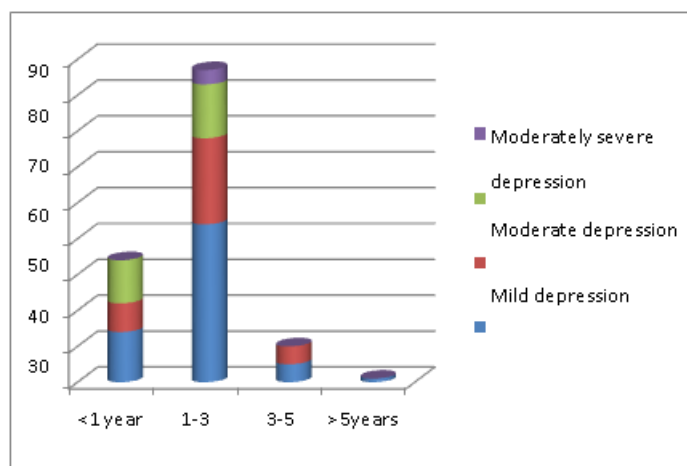| Depressive Symptoms	Patient's gender	No of patients	Percentage
Minimal depression	Male Female Total	49 7 56	87.5 12.5 100
Mild depression	Male Female Total	39 18 57	68.4 31.5 100
Moderate depression	Male Female Total	17 19 36	47.2 52.8 100
Moderately severe depression	Male Female Total	4 11 15	36.7 73.3 100
Severe	Male Female Total	2 2 4	50 50 100

Figure 4: Association of Depressive Symptoms with duration of CKD.

Table 9: Incidence of ADR.

Patients observed with ADR	No of patients	Percentage
Yes	15	8.9
No	153	91.1

Table 10: Suspected ADR in the Study Population.

Adverse Reactions	Number of Patients	Percentage
Gastric problems*	7	46.7
Skin Rashes	2	13.3
Dizziness	3	20
Head ache	2	13.3
Hypersensitivity	1	6.7
Total	15	100

Table 11: Suspected ADR according to the medication in the Study Population.

Suspected medication	Suspected Adverse Reaction	Number	Percentage
Amlodipine	Hypersensitivity reaction	1	33.3
	Headache	1	33.3
	GI Problems	1	33.3
	Total	3	99.9
Furosemide	Dizziness	2	50
	Head ache	1	25
	GI problems	1	25
	Total	4	100
Carvidilol	Dizziness	1	25
	Head ache	1	25
	GI problems	2	50
	Total	4	100
Cilnidipine	Dizziness	2	50
	Skin rashes	2	50
	Total	4	100

Table 12: Hartwing's Severity Assessment in the Study Population.

Severity	Number of Patients	Percent
Mild	11	73.3
Moderate	4	26.7

Table 13: Causality Assessment in the Study Population.

Causality Assessment	No of patients	Percent
Probable	11	73.3
Possible	4	26.7
Total	15	100

Among the 168 patients included in the study, 60.7% are male patients (n=102) and 39.3% are female patients (n=66). The details of gender distribution are represented in **fig: 1.** The **table:2** shows that most of the patients were between 51-65 yrs (n=58). Most of the population were with duration of CKD between 1-3 yrs as shown in **table:3. Table:4 s**hows that most of the patients are with 8-9 drugs. Most of the patients are with low adherence which is depicted in **fig:2**. Majority of the patient with age group 51-65 have low adherence. This is shown in **table:5**. Majority of the male population (n=58) is with low adherence as shown in **fig:3**. In the study population

majority of the patients have mild depression as depicted in **table:6**. Among patient with mild depression majority of the patients were in the age group 51-65 yrs and most of them were males as shown in **table:7** and **table:8**. Majority of the patients is found with mild (n=57) and minimal (n=56) depression. More number of patients with minimal depression, mild depression, moderate depression, moderately severe and severe depression was found in patients with duration of 1-3 years. The association between depressive symptom and duration of CKD is statistically significant. According to the **table:9.** 15 patients are presented with ADR. In the study population majority of the patients were with gastric problems as depicted by **table:10**. Medication observed with ADR are Amplodipine, Furosemide, Carvidilol, Clinidipine as shown in the **table:11**. As depicted in **table:12** Majority of the patients were present with mild ADR(n=11). Causality in most of the patient were probable (n=11) as shown in the **table:13.**

DISCUSSION
The present study set out to assess the patient compliance and depressive symptoms associated with polypharmacy in CKD patients. The study was carried out in the

nephrology department of KR hospital, Mysore over a period of 6 months.

Demographics

Out of 168 patients reviewed, we found that male patients (60.7%) were predominant while comparing to female patients (39.3%). This was concordant with the study result of **Hida M et al**. which was conducted in 579 CKD patients.[3] In this study males were dominant when compared to the opposite class. The result pointed out that the older patients have more incidence of CKD. It is supported with the study conducted by **Suma Prakash et al**. where the study shows that over more than half of those with above 60 years are at more risk in developing CKD.[36][37] On the review of quantity of drugs used in the study population, it was found that 56.2% were prescribed with 8-9 drugs, 22.6% were with 5-7 drugs and 16.7% with 10-11 drugs. This study co-relates with study of **Ankit Sutaria et al.**[5] Her study concludes after the inclusion subjects who were having above 60 years. Patients with multiple medications were classified as those having 5 or more medications per day. It is revealed that majority of the patients were taking multiple drugs and which is equal to or above 8.[38]

Medication Adherence

Out of 168 patients, 45.8% were found to have low adherence and 18.5% patients were highly adhered**. S.Manju et al**.,conducted a cross sectional study on medication adherence associated with polypharmacy in CKD patients.[1] It states that polypharmacy increases the chances of poor adherence. On viewing medication adherence with age group, we found that age group with 51- 65 yrs are low adherent to the medication. Our findings can be strengthened with the help of a study carried out by **Eric.J.Maclaughin et al.**[13] He conducted a study on medication adherence in elderly patients and figures out that age group above 50 yrs are more prominent with low adherences. Inadequate or marginal health literacy is one of the main reasons for non-adherence. Comorbidities, presence of cognitive vision or hearing impairment also leads to low adherence in elderly patients.

In the assessment of medication adherence with gender, we found that low adherence is dominant in male patients. Correlation between medication adherence and gender was found to be non- significant. This can be strengthened with the help of a study conducted by **Siva Kala et al**.[6] The study noted that association between medication adherence and gender is not significant. In contrast to our result, Chironda G et al., conducted a systemic review of literature to identify the factors influencing medication adherence. He found that patient related factors appear to affect adherence of CKD patients. Gender have found to be a determinant in adherence issues. He also found that non-adherence is consistently associated with males.[44]

Adherence to medication in relation with duration of CKD, out of 6 patients who were being reported for 3-5

years, we found that 5 patients are with low adherence. Correlation between medication adherence and duration of CKD found to be 0.091 with a P value of 0.240. **B.Verma et al**., conducted a study to assess the reasons for the non-adherence to medications in CKD and he found that duration of treatment is one of the major reasons for non-adherence.

Depressive Symptoms

Out of 168 patients, 57 patients were found with mild depression. According to **Schayan Schirazian et al**., depression is highly prevalent and is associated with poor QOL and increases mortality rate among adults with CKD.[2]

In our study we found that, the incidence of depression is more among the patients of age group 31-50 years. Association between age group and depressive symptom is observed with P value of 0.01. According to **R.Ahlawat et al**., younger age less than 60 was found to be a significant risk factors for the depression in CKD patients.[10]

In our study, gender had significant association with depressive symptoms. Female patients are observed with more depressive symptoms when compared to male patients. A study conducted by **Andrade CP et al**., supported our result which also showed a significant association between gender and depressive symptoms.[11] However a study conducted by **O.Amira et al**., showed a contrast result to our study in which the association between depressive symptoms and gender was not significant.[12]

In the study population out of 168 patients, 15 patients were observed with ADR. In the study amplodipine had caused ADR in 3 patients that were hypersensitivity reaction (n=1), head ache, GI problem(n=1). 4 patients were affected with ADR due to the administration of furosemide. Because of the close monitoring in CKD patients by dose adjustment the incidence of occurrence of ADR is less.

CONCLUSION

CKD is defined as an irreversible condition with abnormalities of kidney structure or function, present for > 3months, with implication of health. Kidney damage includes a wide range of abnormalities and is observed during clinical assessment. GFR is accepted as the overall index of. Kidney function. It is very difficult to identify CKD in its early stage. Several issues contribute to high prevalence in India. Diabetes and hypertension account for 40%-60% CKD in India. As per Indian Counsil of Medical Research, prevalence of CKD is increased by 6.3%. Due to lifestyle diseases there is a 30% increase in the CKD in US. Smoking, obesity, older age family history also contributes to the development of CKD.In our study male patients with older age are dominant with CKD.

Older patients with CKD use more than 5 medications and have multiple dosage regimen. It affects the adherence behavior in this population and also leads to ADRs. Most of the patients are with poor medication adherence with their physicia ns. In our study also poor medication adherence behaviour is observed. It is the duty of a clinical pharmacist to monitor the adherence of the patients. The pharmacist should make the patients aware about the indications and importance of the medications. Pharmacist medication review, patient counseling, and telephone follow up are some of the methods to improve medication adherence of the patients. Close monitoring and dose adjustment is very much required to avoid drug reaction and its complications. In the study medication adherence shows statistically significant association with age, education, andduration of CKD. Gender showed no association with medication adherence

Depression is prevalent CKD patients and in most of the cases it is under recognized. Reason for low treatment rate is the result of lack of proper controlled trials. Proper treatment is essential before the worsening of the condition. In our study more patients are observed with mild depression. Proper counseling, awareness, early detection of the condition is necessary to prevent the progression of the disease. Depression showed statistically significant association with age, gender, education, duration of CKD.

Pharmacists are important health professionals in counseling and monitoring the patients. They have significant role in educating the patients about the disease and therapy encouraging adherence, explaining about the side effect and adverse drug reaction. Moreover, pharmacist can prevent co- morbidities of the disease and can improve quality of life of patients in their daily. To achieve the desired goal gap between the views of medical professionals, patients and pharmacists have to maintain good relationship healthy communication should be maintained. The occurrence of the disease can be prevented upto an extent if healthcare professionals provide suitable awareness programs regarding the disease and acknowledge the community about its curing measures. It has to be an objective for every healthcare professional including pharmacists to free the society from the health related issues and to provide better quality of life.

REFERENCE

1. S.Manju et al, Medication Adherence associated with polypharmacy.Sr., July, 2016; 46: 3107-11 01 DOI: 10.13040/IJPSR.0975-8232.7(7).3107-11
2. Shayan Shirazian et al. Depression in Chronic Kidney Disease and End Stage Renal Disease: Similarities and differences in Diagnosis, Epidemology, and management. Kidney int Rep., Jan, 2017; 2(1): 2(1): 94-107. DOI: 10.1016/j.ekir.2016.09.005 PMCID:PMC5720531
3. Hida M et al. Age and sex distribution in chronic renal failure patients at dialysis induction PM ID : 3837949
4. S.Praksh et al. Interactin of Aging and CKD. Semin Nephrol, 2009 sEp; 29(5): 497-503.
5. Ankit Staria et al. Multiple medication and Chronic kidney disease in patients aged 60 and older: a pharmacoepidemiollogic perspective Ther Adv Cradiovas Dis., Aug, 2016; 10(4): 242-250.
6. Siva Kala et al. Assessment of knowledge and adherence to therapy among chronic kidney disease International Journal of Medical Science and Public Health, 2019; 8: 3. DOI: 10.5455/ijmph.2019.0101523012019
7. P.P Varma et al. Prevalence of chronic kidney disease in India-Where are we heading?. Indian J Nephol, My-Jun, 2015; 25(133-135) PMCID: PMC4446915 PMID:26060360
8. Chironda G et al. Contributing factors to non adherence among Chronic Kidney Disease patients: A systematic review of literature. Med Clin Rev., 2016; 2: 29. DOI: 10.21767/2471-299x.1000038
9. Arjun D Sinha Clinical Pharmacology of antihypertensive therapy for the treatment of hypertension in CKD. CJSN May, 2019; 14(15): 757-764. DOI: http://doi.org/10.2215/CJN.04330418
10. R. Ahlawat et al Prevalence of depression and its associated factors among patients of chronic kidney disease in a public tertiary care hospital in India: A cross- sectional study. Year, 2018; 29(5): 1165-1173. DOI: 10.4103/1319-2442.243972 PMID: 30381514
11. P.Andrade et al. Evaluation of depressive symptoms in patients with chronic renal failure. JNephrol, 2010; 23(02): 168-174.
12. O. Amira et al.Prevalence symptoms of depression among patients with chronic kidney disease. Year, 2011; 14(4): 460-464. DOI: 10.4103/1119-3077.91756
13. Eric J, et al Assessing medication adherence in elderly: which tools to use in clinical practice?. Drugs Aging, 2005; 2(3): 231-2551170-229X/05/0003-0231