

**A STUDY ON PRESCRIPTION PATTERN OF HYPOGLYCEMIC AGENTS USE IN  
DIABETIC CKD PATIENTS****Silkam A. Sangma\*, Mahadevamma L. and Kyrshanlang Warshong**

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**ABSTRACT**

**Introduction:** Diabetes Mellitus is now recognized as a major chronic public health problem throughout the world. Diabetic Mellitus is the leading cause of chronic kidney disease and a major source of morbidity and mortality in patients with established Chronic Kidney Disease. **Methodology:** This was a Prospective and Observational study in which 80 subjects were enrolled based on the criteria, and was assessed and evaluated by utilised a suitable statistical method. **Results:** Among 80 patients the majority of study subjects 62 (77.5%) were male and 33 (41.3%) were belonged to the age group of 61-70 years out of which 14 of them were obese patients. The prescription pattern showed short acting insulin was prescribed at a higher rate of 20 (15.5%) patients followed by Long acting insulin 18 (14%) and among oral anti-diabetic drugs, Dipeptidyl-peptidase-4 inhibitors 39 (30.2%) with vildagliptin itself prescribed in 19 (14.7%) patients, 2<sup>nd</sup> generation of sulfonylurea 12(9.3%), alpha-glucosidase 06 (4.7%), SGLT2 inhibitor 06 (4.7%) and combination of 2<sup>nd</sup> generation sulfonylurea + biguanide 07 (5.4%). **Conclusion:** Among all the hypoglycemic drugs, the insulin was highly preferred as monotherapy as well as combination therapy over all oral hypoglycemic agents to control the elevated and type -2 glycemic level and vildagliptin accounted for the most commonly prescribed Oral hypoglycemic agents. In the 2<sup>nd</sup> generation of sulphonylureas class, glimepiride and glipizide were mostly prescribed. This study monitored and evaluated toward the achievement of rational drug use.

**KEYWORDS:** In the 2<sup>nd</sup> generation of sulphonylureas class, glimepiride and glipizide were mostly prescribed.

**INTRODUCTION**

The kidneys are a pair of organs that are found on the either side of the spine that are responsible for filtering blood, removing waste and controlling the body's fluid balance. They filter waste materials out of the blood and pass out of the body as urine, regulate blood pressure and the level of water, salts, and minerals in the body and produce hormone that control other body function. Damage to the kidneys can occur in people who have had diabetes for many years particularly if the diabetes is not well control. Chronic Kidney Disease (CKD) is a progressive loss of function over several months to years, characterized by gradual replacement of normal kidney architecture with interstitial fibrosis. CKD is categorized by the level of kidney function, based on Glomerular Filtration Rate (GFR), into stages 1 to 5, with each increasing number indicating a more advanced stage of the disease, as defined by a declining GFR. CKD stage 5, previously referred to as end-stage renal disease (ESRD), occurs when the GFR falls below 15 ml/min per 1.73m<sup>2</sup> body surface area. The patient with stage 5 CKD requiring chronic dialysis or renal transplantation for relief of uremic symptoms is said to have ESRD.<sup>[1]</sup>

CKD development and progression is insidious. Patients with stage 1 or 2 CKD usually do not have symptoms or metabolic derangements seen with stages 3 to 5, such as anaemia, secondary hyperparathyroidism, cardiovascular disease, malnutrition, and fluid and electrolyte abnormalities that are more common as kidney function deteriorates. Uremic symptoms (fatigue, weakness, shortness of breath, mental confusion, nausea, vomiting, bleeding and anorexia) generally absent in stages 1 and 2, minimal during stages 3 and 4, and common in patients with stage 5 CKD who may also experience itching, cold intolerance, weight gain, and peripheral neuropathies.<sup>[2]</sup>

Patients with stage 5 CKD on dialysis are known to take a large number and variety of medications with potential for development of significant medication-related problems. They have multiple co-morbidities and complication also need for a large no. of prescription medications, including those that might alter the rate of progression of decline in kidney function.<sup>[3]</sup>

The KDIGO guidelines define kidney disease as structural or functional abnormalities of the kidneys that have implications for health, and classify kidney disease according to duration, cause, severity of structural and functional abnormalities, and prognosis. CKD is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health," and requires one of two criteria documented or inferred for >3 months: either GFR <60 ml/min/1.73m<sup>2</sup> or markers of kidney damage, including albuminuria. This guideline is designed to apply to a broad population of patients with diabetes and CKD. Assessment of diabetes control is required to achieve glycemic targets.<sup>[4]</sup>

Use of specific glucose lowering agents, such as SGLT2 inhibitors and GLP-1 RA, may have a greater impact in kidney and cardiovascular outcomes in patients with T2D and CKD than in reaching specific HbA1c targets. Lifestyle therapy is the cornerstone of management for patients with T2D and CKD. In addition, metformin and SGLT2i should be used in combination as first-line treatment for all or nearly all patients with an eGFR  $\geq$  30 ml/min per 1.73m<sup>2</sup>. Metformin is a safe, effective, and inexpensive foundation for glycemic control in T2D with modest long-term benefits for the prevention of diabetes complications. SGLT2i have weaker effects on HbA1c, particularly with an eGFR of 30–59 ml/min per 1.73 m<sup>2</sup>, but they have large effective for preventing CKD.

Prescription pattern is to be thoroughly monitored and evaluated to recommend any necessary modification towards achievement of rational drugs use and to avoid unwanted effects and also to ensure optimal patients outcomes. It's explain the extent and profile of drug use, trends, quality of drugs, and compliance with regional, state or national guidelines like standard treatment guideline, usage of drugs from essential medicine list and use of genetic drugs and the purpose of this study is to describe the prescription patterns of selected medication classes and to determine predictors of types of medication used in Diabetic CKD patients. Thus this study will provides an overview of prescription practices on a Diabetic CKD patients and systematic educational efforts in this direction may well prove worthwhile to impact outcomes.

### Methodology

The study was conducted for a period of six months in Sagar Hospital, Bengaluru. A total no. of 80 patients from the Nephrology and Endocrinology department of Sagar Hospital, who satisfied the study criteria and consented to participate in the study were included. The study was conducted with accordance to the international conference on Harmonization-Good Clinical Practice Guidelines. Ethical Committee Clearance was obtained from the board for the protocol to conduct study in the hospital, study procedure and patient's consent form.

Diabetic CKD patients and along with other comorbidities being treated with hypoglycemic agents

were recruited for the study. Pregnant and lactating women, CKD patients without diabetes and patients Aged <18yrs were excluded.

Patients with diabetic condition admitted to the Nephrology department of Sagar Hospital in Bengaluru-during the study period-were screened for the report of diagnosis treatment of hypoglycemic agent use in diabetic CKD patients. Those who met the inclusion and exclusion criteria were enrolled for the study. Follow up were carried from day of admission to the day of discharge of the enrolled patients. After the diagnosis was confirmed by the physician, necessary baseline information such as the socio-demographic details of the patient and details on the visit for the treatment was obtained from the patient Data collection form and even the patient Demographic was also collected. To assess the laboratory parameters were using by Serum creatinine, glycosylated haemoglobin, random blood sugar level, fasting blood sugar level, Urine test, Proteinurea, haemoglobin and to assess the prescription patterns were using drugs name and class of drugs. Data was analysed by using suitable statistical tool.

Data management and statistical analysis were performed using SPSS statistical software version 20.0. Microsoft excel 2010 were used to arranged the data.

### RESULTS

Based on the study criteria, 80 patients were selected and enrolled for the study. Among 80 patients the majority of study subjects 62 (77.5%) were male and 33 (41.3%) were belonged to the age group of 61-70 years out of which 14 of them were obese patients. The prescription pattern showed that majority of patients had more than one antidiabetic medication. Human insulin (short acting insulin) was prescribed at a higher rate of 20 (15.5%) patients followed by insulin glargine (Long acting insulin) 18 (14%) and among oral anti-diabetic drugs, Dipeptidyl-peptidase-4 inhibitors 39 (30.2%) with vildagliptin itself prescribed in 19 (14.7%) patients, 2<sup>nd</sup> generation of sulfonylurea 12(9.3%), alpha-glucosidase 06 (4.7%), SGLT2 inhibitor 06 (4.7%) and combination of 2<sup>nd</sup> generation sulfonylurea + biguanide 07 (5.4%). This study was conducted to assess and evaluate the prescription pattern of hypoglycemic agents used in diabetic chronic kidney disease patients. Among all the hypoglycemic drugs, the short acting insulin was highly preferred over all oral hypoglycemic agents(OHAs) to control the glycemic level and vildagliptin accounted for the most commonly prescribed OHAs. In the 2<sup>nd</sup> generation of sulphonylureas class, glimepiride and glipizide were mostly prescribed. During the course of hospital admission based on prescription pattern, minimum glycemic control agents such as Insulin isophane, Canagliflozin and Miglitol were only prescribed for few patients. Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with metformin and sodium-glucose cotransporter-2 inhibitor and additional drug

therapy as needed for glycemic control. Monitor eGFR in patients treated with metformin. Increase the frequency of monitoring when the eGFR is  $<60\text{ml/min per }1.73\text{m}^2$ . Prescriptions for metformin were lower than expected among patients with mild to moderate CKD.

## DISCUSSION

This study was conducted on the patients who were diagnosed with Diabetic CKD in the Endocrinology and Nephrology department of Sagar Hospitals, Bengaluru. The Patients were enrolled on the basis of complains of Diabetes along with CKD and analyzed for the hypoglycemic agents prescribed. Studies on anti-diabetics drug prescription and analysis the medication can lead to the promotion of rational drug therapy and effective treatment that eventually can help to achieve optimal glycemic control and therapy adherence, which reduce the morbidity and mortality in diabetic chronic kidney disease patients.

### Gender

In the current study, a total of 80 patients were involved out of which 62 were male and 18 were females giving a percentage of 77.5% and 22.5% respectively. This indicate that male were predominance which is similar to result of other studies.

### Age

Age distribution of the given population showed that 5.0% of patients belong to the age group of 31-40 years, 8.8% in the age group of 41-50 years, 21.3% in the age group of 51-60 years, majority of patients 41.3% were belonged to the age group of 61-70 years, 22.5% in the age group of 71-80 years and least no. of patients 1.3% were belonged to the age group of 81-90 years. This implies that higher incidence of Diabetic CKD and its complication were found in the age group of 61-70 years and thereby appropriate prescribing treatment are required in elderly people to prevent further complication of disease.

### BMI

During our research, only 47.5% of patients were accurately calculated for their BMI, and almost 52.5% of data was not clear. Out of 47.5%, 19 (23.8%) were identified at a range of 30 to 39.9 which indicates that the patients were obese.

### Type of DM

In our study, we have observed that 73 (91.3%) of patients were diagnosed with type-2 diabetes mellitus and only 7(8.7%) patients were diagnosed with type-I diabetes. This indicates that type 2 DM is more prevalence than type 1 in Diabetic Chronic Kidney Disease patients.

### Parameters

In our study, distribution of subjects according to parameters determination showed that serum creatinine when  $>1.21\text{mg/dl}$  gives 97.5%, GRBS when  $>200$  shows

66.3%, FBS when  $>100$  shows 71.3%, Hb when  $<13.5\text{g/dl}$  shows 81.3% followed by HbA1c when  $>5.6$  identified as 92.5% respectively.

### Serum creatinine

In our study, the distribution of the subjects according to serum creatinine level evaluated when  $>1.21$  is 78 (97.5%) and  $<1.21$  is 2 (2.5%). This increase in the serum creatinine occurred during treatment initiation and later stabilized within 2-4 weeks in the setting of normal sodium and fluid intake. Therefore patients was monitored for symptomatic hypotension, hyperkalemia and excessive rise in serum creatinine level. Distribution of serum creatinine according to gender observed that male genders are more prone to serum creatinine  $>1.21\text{mg/dl}$  than females implies that males (75.0%) are at more risks than females (22.5%).

### HbA1c

During study period, all patients had undergone HbA1c evaluation, we have observed that almost 92.50% of patients were resulted HbA1c values  $>5.6$ . Glycosylated hemoglobin A1c (HbA1c) is most commonly measured as an indicator of glycemic control during the preceding 2-3 months because it comprises the majority of HbA1c and is the least affected by recent fluctuations in blood glucose. Out of 80 patients, 6 (7.5%) had good glycemic control (HbA1c  $<5.6\%$ ) and 74 (92.5%) had HbA1c level greater. This represent that HbA1c is the standard of care for the monitoring and evaluation of optimal glycemic control. Distribution of HbA1c according to gender showed that male genders (70.0%) are more prone to HbA1c  $>5.6$  than females (22.5%) indicates that male have a greater risk of hyperglycemia.

### GRBS and FBS

In addition to long term glycemic control, daily glycemic monitoring with CGM (continuous glucose monitoring) or SMBG (self monitoring of blood glucose) may help prevent hypoglycemia and improve glycemic control when anti-hyperglycemic therapies associated with risk of hypoglycemia are used and out of 80 patients, 27 (33.8%) had good glycemic control (GRBS  $<200\text{mg/dl}$ ) and 53 (66.3%) had GRBS greater and 3 (3.8%) of patients had good FBS control ( $<100\text{mg/dl}$ ), 57 (71.3%) had FBS of greater than the normal range ( $>100\text{mg/dl}$ ) and it was not assessed in 20 patients (25.0%). Distribution of GRBS and FBS according to gender also shown that males 50.0% of  $>200\text{ mg/dl}$  GRBS and 56.2% of  $>100\text{mg/dl}$  are more susceptible than females 16.2% of  $>\text{GRBS}$  and 15.0% of  $>100\text{mg/dl}$  FBS in developing hyperglycemia.

### Drug's class

The distribution of subjects according to drug class showed that majority of patients were prescribed with DPP-4 inhibitor class of drugs 39 (30.2%) followed by short acting insulin class of drugs 20 (15.5%), long acting insulin 18 (14.0%), 2<sup>nd</sup> generation of sulfonylureas 12 (9.3%). In the 2<sup>nd</sup> generation of sulfonylureas class,

glimepiride and glipizide were mostly prescribed. Other classes of hypoglycemic drugs prescribed were rapid acting insulin (3.1%), combination insulin (4.7%), intermediate acting insulin (0.8%) among oral hypoglycemic agents SGLT2 inhibitor (4.7%), 2<sup>nd</sup> generation sulfonylurea + biguanide 7 (5.4%), alpha-glucosidase inhibitor (4.7%), biguanide (1.6%) and meglitinide (0.8%).

### Prescribed drugs

Human insulin was prescribed at higher rate (15.5%), followed by vildagliptin (14.7%), insulin glargine (14%) and linagliptin (10.9%). This indicate that insulin was highly preferred over all oral hypoglycemic agents(OHAs) to control the glycemic level and vildagliptin accounted for the most commonly prescribed OHAs.

### Distribution of drugs according to type of DM

Our study showed that majority of type-II diabetic chronic disease patients were prescribed with vildagliptin,<sup>[19]</sup> human insulin,<sup>[16]</sup> insulin glargine,<sup>[16]</sup> linagliptin<sup>[14]</sup> and minority of patients with type-II DM were prescribed with combination of glimepiride + metformin + voglibose (1), insulin aspart + insulin aspart protamide (1), insulin degludec (1), insulin isophane (1), miglitol (1), and repaglinide (1). It also showed that no oral hypoglycemic agents (OHA's) were prescribed in Type-I diabetic chronic disease patients.

### CONCLUSION

Diabetic Nephropathy is a serious kidney-related complication of type 1 diabetes and type 2 diabetes. It is also called diabetic kidney disease. About 25% of people with diabetes eventually develop kidney disease. The best way to prevent or delay diabetic nephropathy is by maintaining a healthy lifestyle and treating your diabetes, high blood pressure and glycemic control. In our study, a total of 80 patients subjected were enrolled, assessed and evaluate for the diabetic nephropathy, obesity, edema to manipulate a test for each individual manifestation. The majority of study subjects were male belonged to the age group 61-70 years out of which 14 of them were obese. Patient's characteristics was assessed and evaluated and the study showed that prevalence of males was more when compared to women. Patients were evaluated and diagnosed on basis of few commonly observed symptoms of swelling of limbs, hands, face, ankles, fatiguability, worsening blood pressure control, shortness of breath, loss of appetite. Laboratory values of patients were Serum creatinine, GRBS, FBS, HbA1c. These parameters were chosen as they are likely to show abnormalities in serum creatinine, BMI and GRBS for diabetic nephropathy.

Prescribing pattern was thoroughly monitored and evaluated toward the achievement of rational drug use and to identify the outcomes of hypoglycemic agents. Our data indicating rational prescribing practices of hypoglycemic agents in diabetic chronic kidney disease

patients but factors like patient's compliance and education regarding the disease and lifestyle modification are also important to achieve the optimal glycemic control that needs further investigation. The main supportive treatment were Haemodialysis which was conducted maximum trice a week in a month. Prescriptions for agents contraindicated in advanced CKD continued to be written in a sizeable fraction of patients. This study was conducted to measure the prevalence of Diabetic CKD, the effects of age and gender on its prevalence and their prone profile in the enrolled subject provide the laboratory data to monitor the status of prescription pattern of hypoglycemic agent and enhance the treatment recommendation in a hospital. This study targets a good contribution for community, society and allows differentiating the treatment regimen of drugs by determining a rationality of prescribing practice of hypoglycemic agent used. This dissertation is crucial significance for clinicians to facilitate empiric management of patients in an adequate rationality prescribed pattern.

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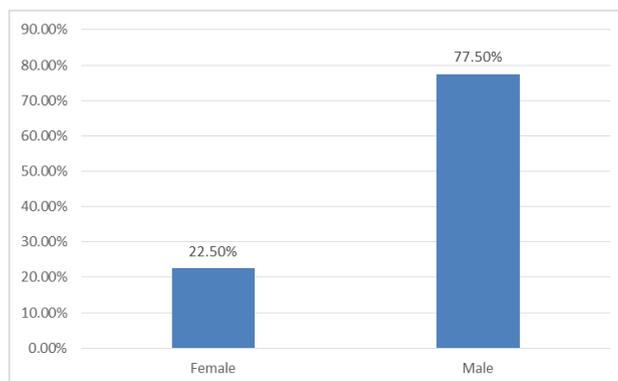
chairman, Institutional ethics committee, Sagar Hospitals Bengaluru.

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**Table no. 01: Distribution of subjects according to gender.**

Gender	Frequency	Percent
Female	18	22.5
Male	62	77.5
<b>Total</b>	<b>80</b>	<b>100.0</b>

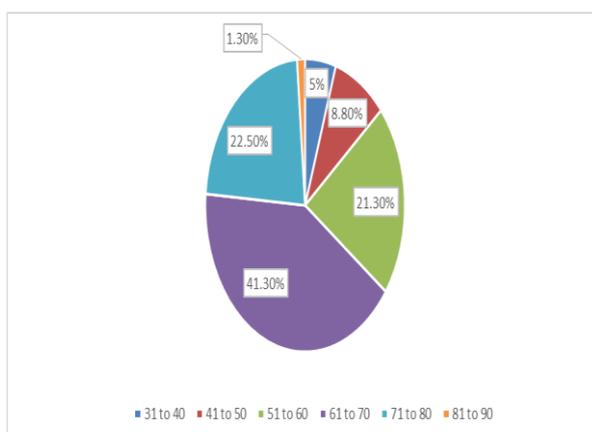


**Figure no. 01: Distribution of subjects according to gender.**

In our study findings, we have observed that majority of patients were male gender only

**Table no. 02: Distribution of subjects according to age group.**

Age group	Frequency	Percent
31 to 40	4	5.0
41 to 50	7	8.8
51 to 60	17	21.3
61 to 70	33	41.3
71 to 80	18	22.5
81 to 90	1	1.3
<b>Total</b>	<b>80</b>	<b>100.0</b>

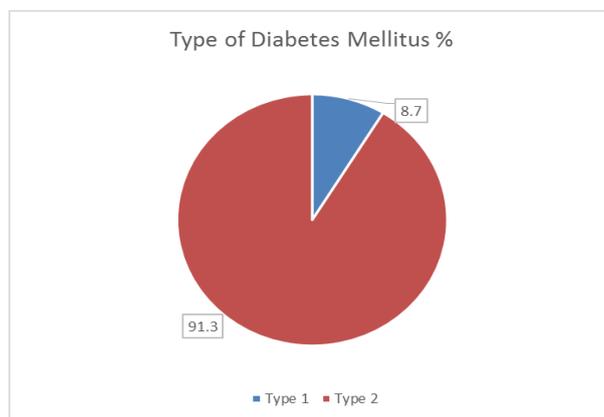


**Figure no. 02: Distribution of subjects according to age group.**

In our study, majority of patients were distributed in the age group of 61 to 70(41.30%) years old, followed by 71 to 80(22.50%) years and least no of patients belonging to the age group 81-90 (1.30%) years.

**Table no 03: Distribution of subjects according to type of diabetes mellitus.**

Type of DM	Frequency	Percent
Type 1	7	8.7
Type 2	73	91.3
<b>Total</b>	<b>80</b>	<b>100.0</b>

**Figure no. 03: Distribution of subjects according to Types of DM.**

In our study, we have observed that 91.3% of patients were diagnosed with type-2 diabetes mellitus followed by type-I diabetes mellitus (8.7%).

**Table no. 04: Distribution of subjects according to drugs prescribed during the study.**

Drug	Frequency	Percent
Canagliflozin	1	.8
Dapagliflozin	2	1.6
Empagliflozin	3	2.3
Glicazide	2	1.6
Glimepiride	4	3.1
Glimepiride+metformin	2	1.6
Glimepiride+metformin+voglibose	1	.8
Glipizide	6	4.7
Glipizide,vildagliptin	1	.8
Glipizide+metformin	5	3.9
Human insulin	20	15.5
Insulin aspart	2	1.6
Insulin aspart+insulin aspart protamide	1	.8
Insulin degludec	1	.8
Insulin glargine	18	14.0
Insulin glulisine	3	2.3
Insulin isophane	1	.8
Insulin isophane+human insulin	5	3.9
Linagliptin	14	10.9
Metformin	2	1.6
Metformin+vildagliptin	3	2.3
Miglitol	1	.8
Repaglinide	1	.8
Tenagliptin	6	4.7
Vildagliptin	19	14.7
Voglibose	5	3.9
<b>Total</b>	<b>129</b>	<b>100.0</b>

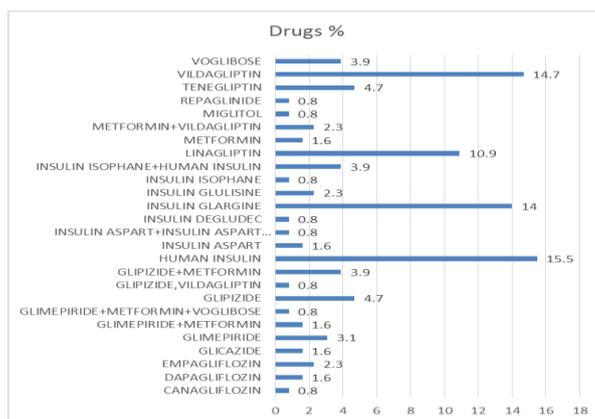


Figure no 04: Distribution of subjects according to drugs prescribed during the study.

In our findings we have observed that, human insulin is prescribed at higher rate (15.5%), followed by vildagliptin (14.7%) and insulin glargine (14%) and insulin isophane (0.8%), insulin degludec (0.8%), repaglinide (0.8%), miglitol (0.8%) were the least.

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