



## Incidence of Use of Contraindicated Oral Hypoglycemic Drugs in New Patients of Diabetic Nephropathy Visiting OPD of Tertiary Care Hospital

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### Introduction

Diabetes is one of the leading causes of chronic renal disease and end stage renal disease<sup>1</sup>. Chronic renal disease is associated with decreased clearance of many oral hypoglycaemic agents (OHAs) and their metabolites, prolonging the duration of exposure to the drug and its metabolites, more so in patients with moderate to severe renal disease<sup>2</sup>. Thus, a diagnosis of renal disease in patients with diabetes merits attention to the revision of the drug therapy of the patient. But, managing hyperglycemia in CKD patients is difficult, partly due to the complexity involved in these patients, and partly due to less data supporting benefits of strict glycaemic control<sup>3</sup>. In spite of this, there is major use of contraindicated oral hypoglycaemic agents in diabetic nephropathy.

### Aims and Objective

In this study, we are focusing on studying the incidence of use of non-recommended Oral Hypoglycaemic drugs in new patients of diabetic nephropathy visiting opd of tertiary care hospital.

### Materials and Methods

A total 600 already diagnosed patients of diabetic nephropathy who visited OPD were recruited in this retrospective, cross-sectional study and were evaluated for use of OHAs according to their medical prescription.

### Results

Of 600 diabetic nephropathy patients, 300 were men and 300 were women. Out of them, 62% were taking contraindicated OHAs according to their respective CKD stage.

STAGES OF CKD		
GRADE 1	Normal/High	>90ml/min
GRADE 2	Mild decreased	60-89ml/min
GRADE 3a	Mild to Moderate decreased	45-59ml/min
GRADE 3b	Moderate to severely decreased	30-44ml/min
GRADE 4	Severely decreased	15-29ml/min
GRADE 5	Kidney failure	<15ml/min

STAGES	MONOTHERAPY	COMBINATION THERAPY
GRADE 1	NIL	NIL
GRADE 2	NIL	NIL
GRADE 3a	NIL	NIL
GRADE 3b	<ul style="list-style-type: none"> <li>METFORMIN (33)</li> </ul>	<ul style="list-style-type: none"> <li>METFORMIN+ GLIMEPIRIDE (36)</li> </ul>
GRADE 4	<ul style="list-style-type: none"> <li>GLIMEPIRIDE (31)</li> </ul>	<ul style="list-style-type: none"> <li>METFORMIN+ GLIMEPIRIDE+ ACARBOSE (20)</li> </ul>
GRADE 5	<ul style="list-style-type: none"> <li>GLIMEPIRIDE (29)</li> <li>METFORMIN (27)</li> <li>ACARBOSE (11)</li> <li>SITAGLIPTIN (18)</li> </ul>	<ul style="list-style-type: none"> <li>METFORMIN+ GLIMEPIRIDE (31)</li> <li>METFORMIN+ GLIMEPIRIDE+ PIOGLITAZONE (28)</li> <li>METFORMIN+ GLIMEPIRIDE (43)</li> </ul>
	NIL	

CLASS AND MEDICATION	DOSE ADJUSTMENT BASED ON eGFR
<b>Biguanide</b> <ul style="list-style-type: none"> <li>Metformin</li> </ul>	USA prescribing information: contraindication for men with serum creatinine =1.5mg/dL and women with serum creatinine = 1.4mg/dL UK guideline allows metformin in patients with eGFR>30ml/min/1.73m <sup>2</sup> KDIGO recommends metformin in patients with eGFR>45ml/min/1.73m <sup>2</sup>
<b>Sulfonylureas</b> <ul style="list-style-type: none"> <li>Glipizide</li> <li>Glimepiride</li> <li>Gliclazide</li> <li>Glyburide or glibenclamide</li> </ul>	No dose adjustment required Initiate conservatively at 1mg daily. Avoid use if eGFR<60ml/min/1.73m <sup>2</sup> Reduce dose if eGFR<30ml/min/1.73m <sup>2</sup> . Not recommended if eGFR<15ml/min/1.73m <sup>2</sup> . Avoid use in patients with eGFR<60ml/min/1.73m <sup>2</sup>
<b>Meglitinides</b> <ul style="list-style-type: none"> <li>Repaglinide</li> <li>Nateglinide</li> </ul>	Initial dose of 0.5mg before meals when eGFR<30ml/min/1.73m <sup>2</sup> . Caution when used with eGFR<30ml/min/1.73m <sup>2</sup> . Initiate with 60mg before meals
<b>a-Glucosidase inhibitors</b> <ul style="list-style-type: none"> <li>Acarbose</li> <li>Miglitol</li> </ul>	Avoid if eGFR<30ml/min/1.73m <sup>2</sup> . Avoid if eGFR<30ml/min/1.73m <sup>2</sup> .
<b>Thiazolidinediones</b> <ul style="list-style-type: none"> <li>Pioglitazone</li> </ul>	No dose adjustment required. Use with caution in patients with CKD and hypervolemia.

CLASS AND MEDICATION	DOSE ADJUSTMENT BASED ON eGFR
<b>GLP-1 receptor agonists</b> <ul style="list-style-type: none"> <li>• Exenatide</li> <li>• Lixisenatide</li> <li>• Liraglutide</li> </ul>	Avoid if eGFR<30ml/min/1.73m <sup>2</sup> . When eGFR between 30 and 50ml/min/1.73m <sup>2</sup> dose should not exceed 5mcg  Avoid if eGFR<50ml/min/1.73m <sup>2</sup> .  Avoid if eGFR<60ml/min/1.73m <sup>2</sup> .
<b>DPP-4 inhibitors</b> <ul style="list-style-type: none"> <li>• Sitagliptin</li> <li>• Saxagliptin</li> <li>• Alogliptin</li> <li>• Linagliptin</li> </ul>	Sitagliptin and saxagliptin dose adjustment required based on eGFR.  100mg daily if eGFR<50ml/min/1.73m <sup>2</sup> .  50mg daily if eGFR 30-50ml/min/1.73m <sup>2</sup> .  25mg daily if eGFR<30ml/min/1.73m <sup>2</sup> .  5mg daily if eGFR<50ml/min/1.73m <sup>2</sup> .  2.5mg daily if eGFR<50ml/min/1.73m <sup>2</sup> .  1.25mg per day when eGFR 30-60ml/min/1.73m <sup>2</sup> , and for those patients with eGFR<30ml/min/1.73m <sup>2</sup> or hemodialysis, the dose should not exceed 6.25mg/day.  No dose adjustment required
<b>SGLT-2 inhibitors</b> <ul style="list-style-type: none"> <li>• Canagliflozin</li> <li>• Dapagliflozin</li> </ul>	No dose adjustment required if eGFR<60ml/min/1.73m <sup>2</sup> .  100mg daily if eGFR 45-59ml/min/1.73m <sup>2</sup> .  Avoid use if eGFR<60ml/min/1.73m <sup>2</sup> , and discontinue use if eGFR<45ml/min/1.73m <sup>2</sup>

## Discussion

Many studies of antidiabetic drugs have excluded people with CKD. So, we lack solid evidence on the effectiveness and safety of these drugs<sup>5</sup>. Managing hyperglycemia in diabetic nephropathy patients is difficult because of decreased GFR and its interference with the clearance and metabolism of antidiabetic agents and insulin resulting in hyperglycemic peaks and hypoglycemia. Therefore, Physicians should reassess the prescriptions frequently and adjust the doses to keep glycemia within normal range to reduce the progression of disease, improving quality of life and minimizing comorbidities, especially to avoid hypoglycemia, which is associated with increased cardiovascular risks<sup>4</sup>.

## Conclusion

CKD is a common complication in T2DM. In these patients, use of Oral Hypoglycemic Agents is more complex than non-CKD patients. A good number of diabetic nephropathy patients are still treated with contraindicated OHAs with their respective renal function.

## References

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