World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

INDIVIDUALIZATION OF ORAL HYPOGLYCEMIC AGENTS IN GERIATRIC DIABETIC PATIENTS

Shaimol T.*, Anilasree B. P., Nahja Rosy K.E., Minhaj Alavi, Najwa Usman Uruniyan paramban, Mohamed Sameer C. and G. Babu

Devaki Amma Memorial College of Pharmacy, Malappuram, Kerala, India.

Corresponding Author: Shaimol T.
Devaki Amma Memorial College of Pharmacy, Malappuram, Kerala, India.

Article Received on 26/09/2022 **Article Revised on 16/10/2022** **Article Accepted on 06/10/2022**

ABSTRACT

Aim: Individualisation of OHA in geriatric diabetic patients. **Objectives**: To analyze drug prescription pattern for oral OHA in geriatric diabetic patients, To observe the prevalence of comorbidities among geriatric diabetic patients, To find any variation between the prescribed medications and individualized medications plan, Identification of glycemic control targets in consideration to individual patient characteristics. **Methodology:** A Retrospective observational study was conducted at PVS Hospital (P) Ltd, Calicut. From January 2021 to June 2021. Case sheet of geriatric diabetic patients from study site, Data collection form (Annexure I, II, III), Literature relevant to the study and guideline for antidiabetic agents in geriatric patients were collected.**Study Procedure:** Diabetic patients of age 60 and above with or without comorbid conditions were identified. The drug prescription of oral antidiabetic drugs in Type2 DM geriatric patients is analysed. The sociodemographic features of diabetic geriatric patients are identified and analyzed On-going systematic criteria-based evaluation of drug used in individual patient level. Individualized dose for the oral hypoglycaemic agents for patient is determined using guidelines and is compared with the doses given to the patient; the variation will be evaluated and assessed. Found out the prevalence of comorbidities in the patients.Analysed the variation between prescribed dose and individualised dose. Identified the glycemic control targets in individual patient**. Results:** The data of 100 diabetic geriatric patients were collected and analysed. The gender analysis showed that 55 patients (55%) were male and 45 patients (45%) were female. In this study, out of 100 patients who were treated with antidiabetic drugs all of them were Type 2 diabetic patients (non-insulin dependent diabetes mellitus) above age of 60 that reflect the increasing prevalence of Type 2 diabetes mellitus in our region. The average number of Oral Hypoglycemic Agents per prescription in this study was 1.46. Biguanides was the most commonly used class with 45.21% of total OHA given. In Fixed Drug Combinations Biguanide and Sulfonylureas are predominant with 28.77%. Biguanide and Sulfonylurea combination makes second most OHA utilisation after Biguanide monotherapy. Metformin was the mostly used drug in our study with a total of 45.21% among monotherapy and in all the combinations used. Metformin and Glimepiride were the mostly used combination drugs 26.71%. In case of Newer OHA DPP4 Inhibitors, its usage as a monotherapy is low (4.11%) but as combination with Biguanide it is higher (8.90%). In our study only 10.26% of the drug was in generic name, WHO Essential Medicine and NLEM was 75.55% and 73.33%. The most common comorbidity seen was hypertension with Type 2 DM in geriatric patients. Patients with diabetes without comorbidity were younger. Patients with only diabetes related comorbidity was higher in males compared to females but non diabetes related comorbidity was found to be higher in females. Metformin should be strictly discontinued in patients with eGFR <30ml/min/1.73 m^2 as it causes lactic acidosis and 88% of the patients with this eGFR level were prescribed with metformin. 36.36% of the cases with eGFR 30-44ml/min/1.73 m^2 were prescribed with varied dose. Similarly, 46.67% and 13.95% in varied dose was observed in eGFR level 45-59ml/min/1.73 $m^2$and >60ml/min/1.73 m^2respectively. A total of 5 Sitagliptin prescription was found in study given as monotherapy and combination therapy. 3 of them had Cl_{Cr} >50 ml/min and all of them had dose given below 100mg/day. 2 patients had Cl_{Cr}<30 and both were given Sitagliptin above max recommended dose. The total patients were grouped into 2 categories based on eGFR level <30-59ml/min/1.73 m^2 – Of 7 prescriptions of Vildagliptin, all were contraindicated. >60ml/min/1.73 m^2– Out of 4 cases prescribed with Vildagliptin, one was contraindicated. The maximum dose of Teneligliptinin geriatric patients is 20-40 mg. Out of the total cases, 3 prescriptions had Teneligliptin given as monotherapy and combination and it is given according to the guidelines. The geriatric doses of Glimepiride, Glipizide and Gliclazide is1mg – 8mg per day, 2.5-80 mg per day and 320 mg per day. Gliclazide can be given for the patients with eGFR ≥30ml/min/1.73 m^2. The maximum daily dose of Voglibose in geriatric patient is 0.6 mg. Of the 100 studied cases of geriatric type2 Diabetes Mellitus cases we grouped them into 3 categories based on the framework for treatment goals for diabetes in older adults. They classified the patients into healthy, intermediate/complex and very complex categories based on the patient characteristics and their HbA1C goals. Based on this categorization 21% were healthy, 45% were intermediate and 34% belonged to the very complex class. In healthy category 57.14% were from age group 60-69 years, 19% from 70-79 years and 5% from 80-89 years. In intermediate 60% were from age group 60-69 years, 28.88% from 70-79 years, 6.66% from 80-89 years, 4.44% from >90 years. In very complex 41.17% were from 60-69 years, 35.29% were from 70-79 years, 20.58% were from 8089 years and 3% were from >90 years. According to the suggested HbA1c goals given above the patients were further classified into patients with controlled (65%) and patients with uncontrolled diabetes (35%). In healthy 7(33.33%) patients had controlled and 14(66.66%) patients had uncontrolled diabetes. In intermediate 28(62.22%) patients had controlled and 17 (37.77%) had uncontrolled diabetes. In very complex 31(91.17%) patients had controlled and 3 (8.82%) had uncontrolled diabetes. **Conclusion:** The study conducted observed the prescribing pattern of OHA, Prevalence of comorbidities, Dose adjustment and Glycemic target in geriatric type 2 diabetes mellitus. Study showed that both men and women are at high risk of T2DM. Metformin was the mostly prescribed OHA both in monotherapy and combination therapy. Prescription trend was moving towards combination therapy especially two-drug therapy. Hypertension was the most common comorbidity. Dose adjustment is needed for most of the patients with low eGFR and more than half of the patients had controlled glycemic level. Geriatric diabetics need drug dosage adjustment.

KEYWORDS: Diabetes, Individualisation of Therapy, OHA, Geriatrics.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia and high glycated heamoglobin with or without glycosuria. Glucose metabolism disorder (GMD) results from a defect in insulin secretion by the pancreas, insulin action on the target tissues (or insulin resistance), or both.

The two major classifications of diabetes mellitus are
Type 1 (insulin deficient)
Type 2 (combined insulin resistance and relative deficiency in insulin secretion).

Diabetes in elderly population
Definition in old people is similar to the one of other people, which means

Fasting glycemia ≥126 mg/dl (7.0 mmol/L)

The definition of elderly is a subject of controversies. In general, a person is considered as old if his/her civil age is ≥ 60 or 65 years old.

Older people with diabetes have higher rates of conditions that might impair ability to self-manage diabetes compared with younger people.

Older people are at higher risk of hypoglycemia, so medication regimens should aim to avoid hypoglycemia.

Pathophysiology
The primary pathophysiological abnormality in the majority of individuals that develop type 2 diabetes is insulin resistance. Insulin resistance develops when the insulin receptor on the surface of muscle and other cells change shape.
This results in an inability of the insulin molecule to attach to the receptor opening the glucose channel, which prevents the uptake of glucose by the cells.

Pharmacological therapy
In elderly patients receiving medication, there are few data that address the most appropriate glycemic targets.

The goals to be determined in the management of glycemic control and risk factors should be based on both the general health status and the predicted life span of the individual.

Comorbidities in older people with diabetes
The most common comorbidities were found to be hypertension (32%), cardiovascular disorders, renal disorder, stroke, and lung disorders , liver disorders, neurological disorders, gastric disorders, dyslipidemia, cancer, depression and diabetic complications.

Individualization of therapy
It is a current trend in health care, particularly for chronic diseases, and is based on the hope that personalized approaches can ultimately result in improved outcomes.

In type 2 diabetes, the availability of a variety of pharmacological therapies for blood glucose control has significantly increased the complexity involved in managing the condition.

Need of individualization
In the care of patients with diabetes, an individualized approach is especially important because of the multitude of variables involved in decision-making, including therapeutic choices, disease duration, presence of complications and co morbid conditions, and economic factors.

Need of the study
For patients who needs less dose, instead of using wide therapeutic range, the dosage can be selected based on each patient's individual need.
To minimize the incidence of ADRs among the patients.
To improve the efficacy of a drug.

MATERIALS AND METHODS

Aim
Individualization of oral hypoglycemic agents in geriatric diabetic patients.

Objectives
To analyze drug prescription pattern for oral hypoglycemic agents in geriatric diabetic patients.
To observe the prevalence of comorbidities among geriatric diabetic patients.
To find any variation between the prescribed medications and individualized medications plan.
Identification of glycemic control targets in consideration to individual patient characteristics.

Study site: A tertiary care hospital in Calicut, Kerala, India
Study period: 6 months, from January 2021 to June 2021.
Study design: Retrospective observational study
Study Disease: Diabetes mellitus
Study criteria:

Inclusion
Patients with type2 Diabetes Mellitus.
Diabetic patients above the age of 60.
Diabetic patient with or without comorbidity.
Patients taking oral hypoglycemic agents.

Exclusion
Patients with Type 1 Diabetes mellitus only.
Patients taking insulin only.

Study guideline
American diabetes association standards of medical care in diabetes- 2020

Data collection forms: Annexure1, 2 and 3
Study materials
Case sheet of geriatric diabetic patients from study site.

Data collection form - Annexure 1,2 and 3 Standard guidelines for antidiabetic agents in geriatric patients (American diabetes association standards of medical care in diabetes- 2020)

Study procedure

Assessed the patient characteristics. Data was collected from case sheets, case records, medication chart, and laboratory reports.

Diabetic patients of age 60 and above with or without co morbid conditions were identified. The drug prescription of oral ant diabetic drugs in Type 2 DM geriatric patients was analysed.

The demographic features and prescription pattern of OHA in diabetic geriatric patients were identified and analyzed.

Individualized dose for the oral hypoglycaemic agents for patient was determined using guidelines and the doses given to the patient.

Statistical analysis

Descriptive statistics for continuous variables were expressed as mean and standard deviation.

Categorical variables were described as frequencies with percentages for the total sample.

Microsoft Excel® (Microsoft corporation 2013) was used to record and analyze the data.

RESULTS AND DISCUSSION

Prescription Pattern of OHA

Demographic data of the patients

Out of 100 prescription collected 55 patients (55%) were male and 45 patients (45%) were female. Male to female ratio was found to be 1.22:1.

Age distribution of study subjects

The mean age of the study population was found to be 70.74±8.19 years.

Prescribing pattern

In 100 prescription there were 146 anti-diabetic drugs were prescribed. The number of anti-diabetic drugs per prescription varied from one to four and the average number of anti-diabetic drug per prescription was 1.46.

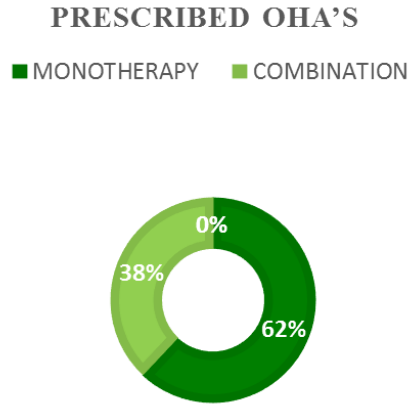

Figure 5.1.2: Distribution of OHA.

Biguanides (45.21%) were the most commonly prescribed monotherapy class followed by combination of Biguanides and Sulfonylureas (28.77%) among the different classes of OHA (Figure 5.1.3).

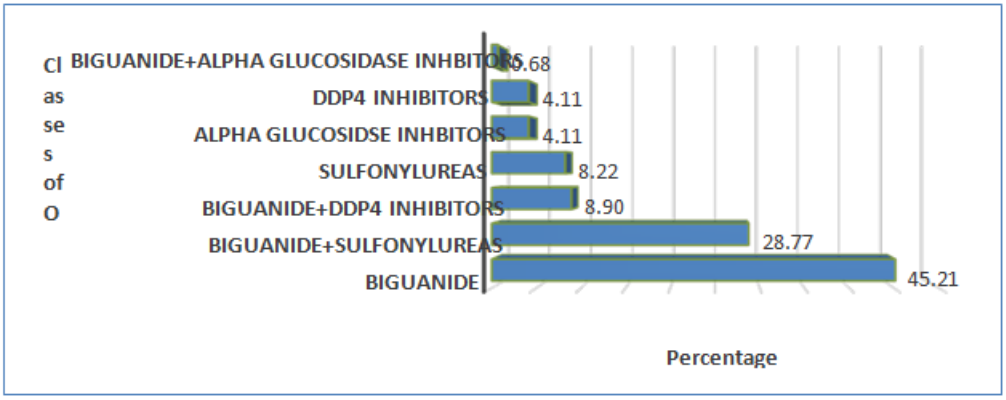

Figure 5.1.3: Percentage of Different class of OHA prescribed.

OHA prescribed as Monotherapy are Sulfonylureas (8.22%), Alpha Glucosidase Inhibitors (4.11%), Dipeptidyl Peptidase 4 Inhibitors (DPP4 inhibitors) (4.11%). Similarly, FDC prescribed were Biguanide and DPP4 inhibitors (8.90%) and Biguanide and Alpha Glucosidase Inhibitor (0.68%).

Metformin was the most common individual OHA Monotherapy to be prescribed (45.21%), and in Fixed Dose Combination Metformin and Glimepiride (26.71%) were mostly prescribed. OHAs given in brand names are listed in Table 5.1.4

Table 5.1.4: OHAs prescribed in brand name.

OHA	Number (out of 146)	Percentage (%)
Glimepiride	7	4.79
Voglibose	6	4.11
Sitagliptin	4	2.74
Glipizide	3	2.05
Gliclazide	2	1.37
Teneligliptine	1	0.68
Vildagliptin	1	0.68
Metformin + Glimepiride	39	26.71
Metformin + Vildagliptin	10	6.85
Metformin + Teneligliptin	2	1.37
Metformin + Gliclazide	2	1.37
Metformin + Voglibose	1	0.68
Metformin + Sitagliptin	1	0.68
Metformin + Glipizide	1	0.68
Metformin	66	45.21

Brand versus generic and selection of essential drugs
In 100 prescription there were 146 OHAs in which 15(10.26%) of them was prescribed in generic name [Table 5.1.5]. Percentage of drugs prescribed from WHO Essential Drug List was 75.55% and National List of Essential Medicines was 73.33%.

Table 5.1.5: Number of generic drugs prescribed in generic name.

Generic Name	Number of Drug
Metformin	8
Voglibose	5
Gliclazide	1
Glimepiride	1

5.1.4 DISCUSSION

In this study, an attempt has been made to describe the current prescribing pattern and trend of anti‑diabetic drug therapy in diabetic patients in a tertiary care hospital Calicut.

In this study, out of 100 patients who were treated with anti‑diabetic drugs all of them were Type 2 diabetic patients (non-insulin dependent diabetes mellitus) above age of 60 that reflect the increasing prevalence of Type 2 diabetes mellitus in our region.

A slightly high proportion of diabetic patients in this study were represented by male similar to the study of Patel B et.al and with other report from India.[21-22]

The average number of Oral Hypoglycemic Agents per prescription in this study was 1.46, which is similar with study done by Agarwal AA et al [16] with 1.40 Anti Diabetic Drugs per prescription. Previous hospital-based studies in India and Abroad has reported 2-5 drugs per prescription,[23-24] our study showed restraint on polypharmacy.

Biguanides was the most commonly used class with 45.21% of total OHA given, similar to studies of Patel B et.al.[15] and Chu et.al.[25] and contrast to studies of Agarwal a A et al where Sulfonylureas being used mostly used. In Fixed Drug Combinations Biguanide and Sulfonylureas are predominant with 28.77% similar to studies of Agarwal AA et al, Patel B et.al and Chu et.al.

Chu et.al mentioned in their studies about the increasing usage of combination therapy for T2DM that can be visibly correlated to our study, where Biguanide and Sulfonylurea combination makes second most OHA utilisation after Biguanide monotherapy.

Metformin was the mostly used drug in our study with a total of 45.21% among monotherapy and in all the combinations used, which is similar to studies of Agarwal AA et al, Patel B et.al and Chu et.al, followed by Glimepiride monotherapy. Metformin and Glimepiride were the mostly used combination drugs 26.71% as like in Patel B et.al.

Metformin is considered to be safer and cost-effective drug over others in terms of hypoglycemia could be the probable reason for this finding. Moreover, additional advantages of Biguanides were discovered such as facilitating weight loss, improving insulin resistance, reducing cardiovascular mortality among obese patients with diabetes, and reducing cancer risk.

The American Diabetic Association regarded metformin as the first line antidiabetic drug as did other guidelines.[25]

In case of Newer OHA DPP4 Inhibitors, its usage as a monotherapy is low (4.11%) but as combination with Biguanide it is higher (8.90%) which is similar to Agarwal AA et.al study.

In our study only 10.26% of the drug was in generic name that correlate with Patel B et al, where they also

find a very low percentage of generic drugs. Similarly, usage of drugs from WHO Essential Medicine and NLEM was 75.55% and 73.33% comparable to Agarwal et.al with 74.2% and 67.1% respectively. But this is in contrast to Patel B et.al where they find it in very low number.

5.2 Prevalence of Comorbidity in Geriatric Patients

Out of the 100 cases we recruited in the study, 90% of cases were geriatrics with comorbidities.

The patients with comorbidities were classified into those with one two and three comorbidities. The most common comorbidities were found to be hypertension (32%), cardiovascular disorders (16.66%), renal disorder (11.66%), stroke (5.83%), and lung disorders (6.66%), liver disorders (1.25%), neurological disorders (1.66%), gastric disorders (1.66%), dyslipidemia (2.91%), cancer (1.66%) and depression (0.41%). The diabetic complications were found to be (1.25%) i.e., diabetic retinopathy, nephropathy, neuropathy and diabetic foot. The percentage distribution is given below:

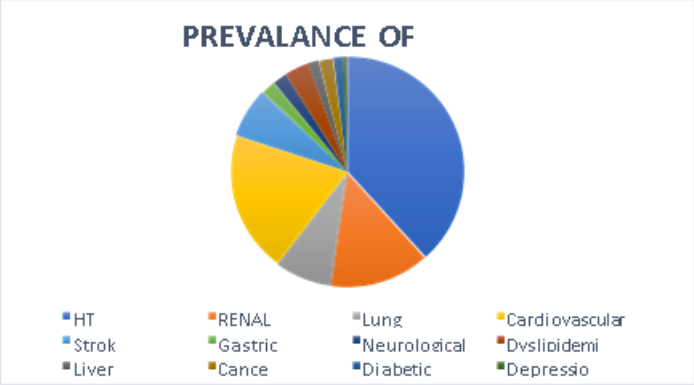

Figure 5.2.1: Prevalence of comorbidity in geriatric diabetic patients.

In 100 cases collected 10% cases presented with no comorbidity in which 7% were male and 3% were female. The patients were further classified into those with one two and three comorbidities. Patients who presented only one comorbidity consisted of 17% of cases (10% male and 7% female), two comorbidities consisted of 40% (20% male and 20% female), and three comorbidities consisted of 33% (18% male and 15% female). The comorbidities were further divided into diabetes related (67.5%) and non-diabetes related (32.5%) comorbidities. Diabetes-related comorbidity included the following chronic conditions: cardiovascular diseases, stroke, retinopathy, nephropathy, diabetic foot and renal disorders. The non-diabetes-related comorbidity was defined as depression, lung diseases Chronic Obstructive Pulmonary Disease (COPD) and asthma, neurological diseases, liver diseases, and cancer. Neurological disease was defined as Parkinson's disease and epilepsy. Cancer was defined as non-Hodgkin disease, stomach cancer, colon cancer, esophagus cancer, lung cancer, skin cancer, breast cancer, and prostate cancer. Gastric diseases were defined as GERD and ulcers. The patients with Diabetes and only diabetes related comorbidity consisted of 24% males and 23% females, patients with diabetes and only diabetes non related comorbidity consisted of 2% males and 3% females, patients with both type of comorbidities consisted of 21% males and 17% females.

Table 5.2.1: Patient characteristics of patients with diabetes for the presence of comorbidity and type of comorbidity.

NUMBER OF COMORBIDITIES	DM ONLY	DM+ ANY COMORBIDITY				TYPE OF COMORBIDTY	
		1	2	3	DM+ only dm related comorbidity	DM+ only dm non related comorbidity	DM+ both types of comorbidities
SEX							
MALE	7%	10%	20%	18%	24%	2%	21%
FEMALE	3%	7%	20%	15%	23%	3%	17%

5.2.1 Discussion

The most common comorbidity seen was hypertension with Type 2 DM in geriatric patients. It was similar to a study conducted by Bela Patel *et.al* [15]. In the patients having comorbidities, diabetes related comorbidities had a higher prevalence rate than non-diabetes related comorbidities. The predominance of hypertension and cardiovascular diseases may be due to the fact that Diabetes Mellitus is a risk factor of Atherosclerosis and hypertension.[15]

Patients with diabetes without comorbidity were younger and were more likely to be male which correlates to the study conducted by Jeroen N Struijs *et.al*[10]. Patients

with only diabetes related comorbidity was higher in males compared to females but non diabetes related comorbidity was found to be higher in females. Whereas the percentage was higher in males when both types of comorbidities taken into consideration.

5.3 Analyse Variation Between Prescribed and Individualized Dose

In this study, we attempted to check whether the oral hypoglycemic agents were given according to the geriatric guidelines. Of all the given OHA's, Biguanides, DDP 4 inhibitors and Alpha glucosidase inhibitors and sulfonylureas require dose adjustments in geriatric patients according to their patient characteristics.

5.3.1 Biguanides

Metformin

Out of 100 cases, 91 prescriptions contain metformin as monotherapy and combination. The guideline emphasized dose adjustment based on eGFR of the patients. The patients were grouped according to eGFR as in Table 5.3.1. The required dose adjustment is given below.[2]

Table 5.3.1: Dose adjustment of Metformin in geriatric Type 2 DM patients based on eGFR.

eGFR (ml/min/1.73 m^2)	Required dose adjustment
<30	Metformin contraindicated
30-44	500 mg-1000 mg max per day
45-59	1000 mg-2000 mg max per day
≥60	2500 mg max per day

In 22 patients with eGFR <30ml/min/1.73 m^2, all were given metformin which is contraindicated. In 11 patients with eGFR 30-44ml/min/1.73 m^2, 4 (36.36%) prescriptions were contraindicated. In 15 patients with eGFR 45-59ml/min/1.73 m^2, 7 (46.67%) prescriptions were contraindicated. In 43 patients with eGFR ≥60 ml/min/1.73 m^2, 6 (13.95%) prescriptions were contraindicated.

Table 5.3.2: Percentage of prescription contraindicated to metformin.

eGFR (ml/min/1.73 m^2)	<30	30-44	45-59	≥60
Total prescriptions	25	13	15	47
Prescriptions with metformin	22	11	15	43
No. of prescriptions CI to metformin	22(88%)	4(36.36%)	7(46.67%)	6(13.95%)

Metformin causes weight loss and hence it is contraindicated in underweight patients.[26] But 21 underweight patients were given metformin in this study.

5.3.2 Dipeptidyl Peptidase 4 Inhibitors

Sitagliptin

The patients were categorized based on Creatinine clearance as in Table 6[2].Maximum Sitagliptin dose for geriatric T2DM patients is listed below.

Table 5.3.3: Sitagliptin geriatric dose.

Creatinine clearance	Max geriatric dose
<30ml/min	25mg / day
30-50ml/min	50mg/day
>50ml/min	100mg/day

A total of 5 Sitagliptin prescription was found in study given as monotherapy and combination therapy. 3 of them had Cl_{Cr} >50 ml/min and all of them had dose given below 100mg/day. 2 patients had Cl_{Cr}<30 and both were given Sitagliptin above max recommended dose.

Vildagliptin

The total patients were grouped into 2 categories based on eGFR level. [28]

<30-59ml/min/1.73 m^2 – Of 7 prescriptions of Vildagliptin, all were contraindicated.

>60ml/min/1.73 m^2– Out of 4 cases prescribed with Vildagliptin, one was contraindicated.

Teneligliptin

The maximum dose of Teneligliptinin geriatric patients is 20-40 mg. Out of the total cases, 3 prescriptions had Teneligliptin given as monotherapy and combination and it is given according to the guidelines.

5.3.3 Sulfonylureas

The drugs given under the class were Glimepiride, Glipizide and Gliclazide. The geriatric doses of Glimepiride, Glipizide and Gliclazide is1mg – 8mg per day, 2.5-80 mg per day and 320 mg per day [11, 27]. Gliclazide can be given for the patients with eGFR ≥30ml/min/1.73 m^2.

Sulfonylureas have an ADR of weight gain. Therefore, it is contraindicated in overweight patients [17]. But in our study, 16 overweight patients were prescribed with Sulfonylureas.

5.3.4 Alpha Glucosidase Inhibitors

Voglibose

The maximum daily dose in geriatric patient is 0.6 mg. Usually it is recommended for patients with FBS <140mg/dl.[29] Out of 7 prescriptions of voglibose, 4 of

them did not exceed the maximum geriatric doses, but their FBS were above 140mg/dl.

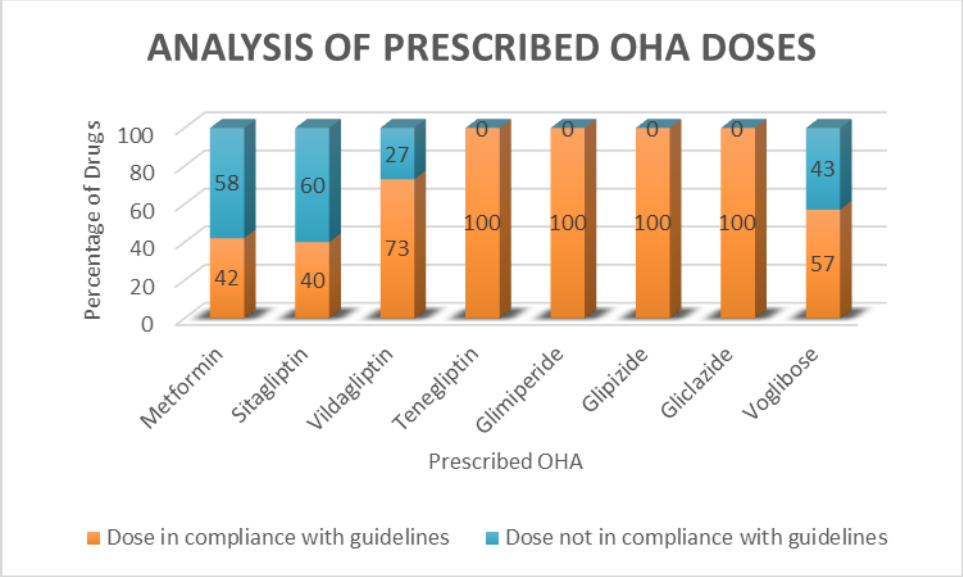

Figure 5.3.1 Analysis of prescribed OHA doses.

5.3.5 Discussion

Biguanides

Metformin typically lowers fasting blood glucose by 20% and A1C levels by 1-2%. It is the first line therapy for diabetes mellitus and it is mostly preferred for overweight patients. The main concern with the use of metformin in older adults is decline in renal function in association with aging. Older patients specifically those ≥80 years, metformin is not recommended until normal renal function is documented.

Metformin should be strictly discontinued in patients with eGFR <30ml/min/1.73 m^2 as it causes lactic acidosis and 88% of the patients with this eGFR level were prescribed with metformin. 36.36% of the cases with eGFR 30-44ml/min/1.73 m^2 were prescribed with varied dose. Similarly, 46.67% and 13.95% in varied dose was observed in eGFR level 45-59ml/min/1.73 $m^2$and >60ml/min/1.73 m^2respectively.

Metformin was prescribed in 23% of the patients with metformin who were underweight.[11,17]

Dipeptidyl Peptidase 4 Inhibitors

It is the first line agent for elderly patients who are contraindicated with metformin. Administration of DDP 4 results in the reduction of HbA1c level from 0.5-0.8%. The drugs prescribed in the study were Sitagliptin, Vildagliptin and Teneligliptin. These groups are weight neutral which combined with the low risk of hypoglycemia. So, it is suitable treatment option for elderly. The doses need to be adjusted based on renal function.

Sitagliptin - 40% of the cases prescribed with Sitagliptin were varied dose.

Vildagliptin – 73% of the cases prescribed with Vildagliptin were varied dose.

Teneligliptin – The drug was prescribed according to the guidelines.[2]

Sulfonylureas

Glimepiride and Glipizide are safer for the older adults, particularly for those patients with renal dysfunction. Previous comparative effectiveness and safety analysis suggested potential advantages of their use as monotherapy. Sulfonylureas given as monotherapy results in the reduction of HbA1c level by1-2%. All the drugs prescribed under Sulfonylureas were according to the guidelines. Sulfonylureas is considered as first line therapy in lean patients as it have a common side effect of weight gain.[17] In this study, 37% of patients prescribed with Sulfonylureas had overweight.

Alpha Glucosidase Inhibitors

The overall effect on HbA1c level is a modest reduction of 0.5-1%.The maximum daily dose in geriatric patient is 0.6 mg, usually 0.2mg tid before food is effective in geriatric. Studies show that 0.6mg Voglibose is ~ 50 mg acarbose. It is associated with less weight gain and a lower frequency of hypoglycemia than Sulfonylureas, and have a better cardiovascular safety profile than other oral agents. Some investigations recommended the use of Voglibose only in patients with active satisfactory fasting glucose level <140 mg/dl with strict diet [29]. 7% of patients prescribed with Voglibose have FBS >140 mg/dl.

5.4 Identification Of Glycemic Control Targets In Considerationto Individual Patient Characterstics

Of the 100 studied cases of geriatric type2 Diabetes Mellitus cases we grouped them into 3 categories based

on the framework for treatment goals for diabetes in older adults as per American Diabetes Association.[26] The care of older adults with diabetes is complicated by their clinical, cognitive, and functional heterogeneity. They classified the patients into healthy, intermediate/ complex and very complex categories based on the patient characteristics and their HbA1C goals as in table 5.4.1

Table 5.4.1: Framework for Hb1AC goals for diabetes in Older Adults from the ADA.

Patient Category and Associated Characterstics	Suggested HBA1C goals (%)
Healthy **Few comorbidities** **Functionally and cognitively intact**	<7.5
Complex/ Intermediate **Multiple chronic co morbidities** **Two or more ADL impairments** **Mild to moderate cognitive impairment**	<8
Very complex/ poor health **End stage chronic illness** **Moderate to severe cognitive impairment**	<8.5

Based on this categorization 21% were healthy, 45% were intermediate and 34% belonged to the very complex class (Fig 5.4.1).In healthy category 57.14% were from age group 60-69 years, 19% from 70-79 years and 5% from 80-89 years. In intermediate 60% were from age group 60-69 years, 28.88% from 70-79 years, 6.66% from 80-89 years, 4.44% from >90 years. In very complex 41.17% were from 60-69 years, 35.29% were from 70-79 years, 20.58% were from 8089 years and 3% were from >90 years.

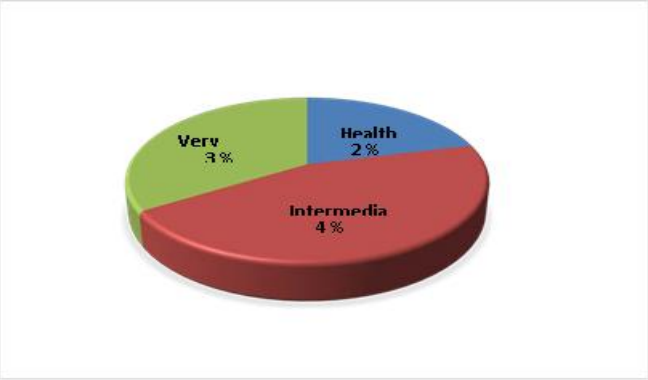

FIG. 5.4.1: Patient classification based on ADA guidelines.

According to the suggested HbA1c goals given above the patients were further classified into patients with controlled (65%) and patients with uncontrolled diabetes (35%). In healthy 7(33.33%) patients had controlled and 14(66.66%) patients had uncontrolled diabetes. In intermediate 28(62.22%) patients had controlled and 17 (37.77%) had uncontrolled diabetes. In very complex 31(91.17%) patients had controlled and 3 (8.82%) had uncontrolled diabetes. The age distribution of each class in shown in the graph below Fig 5.4.2.

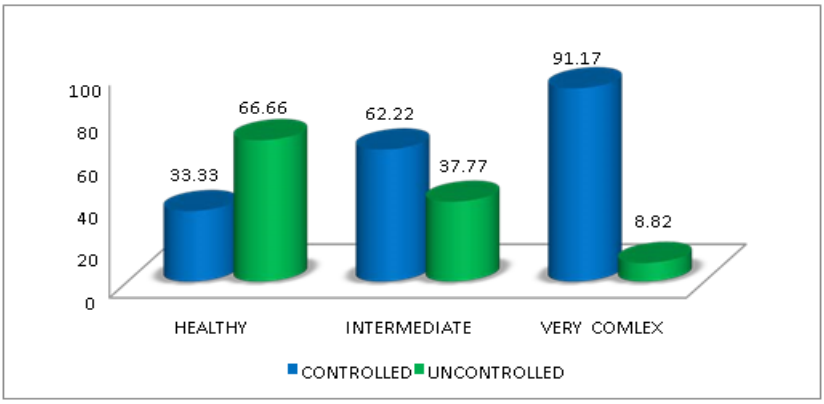

Figure 5.4.2 Percentage of controlled and uncontrolled diabetes in different classes.

Table 5.4.2 Glycemic target in age groups.

AGE (In years)	60-69	70-79	80-89	≥90
Controlled	32(61.53%)	19(63.33%)	12(82%)	2(66.66%)
Uncontrolled	20(38.46%)	11(36.66%)	3(20%)	1(33.33%)

5.4.1 DISCUSSION

Older adults with diabetes require some unique considerations that are not traditionally associated with diabetes care.[2] Both aging and diabetes increase the risk of certain co morbidities including cognitive dysfunction and polypharmacy.[30] In our study we found out that majority of the patients belonged to the intermediate/complex category followed by the very complex/poor health category and individuals belonging to the healthy category were comparatively lower. For those without other major co morbidities an A1C goal of <7.5% whereas for those with multiple chronic co morbidities A1C goal is <8.0% and for those with end stage chronic illnesses A1C goal is <8.5%. The mean HbA1C value was found to be 7.36±2.00 and the mean FBS value was found to be 169.94±79.1 in our study.

The rationale for healthy patients has significant life expectancy and the goal is to prevent future macro vascular and micro vascular complications. In case of intermediate/complex patients they have intermediate life, expectancy and have chance for high treatment burden, they are at risk of hypoglycemia and falls. Very complex/poor health patients have limited life expectancy and the treatment benefit is uncertain, they are also at high risk of hypoglycemia and falls.

Special care is required in prescribing and monitoring pharmacological therapies in older adults. This categorization is mainly done in the geriatric patients as the additional health conditions of these patients may interfere with the ability to perform diabetes self-management, increasing non adherence and treatment errors and increasing the risk of hypoglycemia and poor glycemic control therefore it is essential to conduct a careful and comprehensive approach to the older adults to properly select and implement therapeutic approaches.

A1C remains the gold standard test to assess long term glycemic control in the management of diabetes. It is now also used to diagnosis diabetes[31].However, several factors commonly seen in older adults can falsely raise or lower A1C.[32] In addition, the measurement of A1C is dependent on the length of time the red blood cells (RBCs) circulate in blood.Conditions that falsely increase or decrease HbA1C listed below. [Table 5.4.3]

Table 5.4.3: Conditions that falsely increase or decrease A1C.

Condition	Possible Mechanism	False Change IN A1C
Age	Increased insulin resistance	↑
Iron deficiency anemia	Decreased RBC turnover, longer glycation exposure	↑
Hemolytic anemia, sickle cell anemia or thalassemia	Increased RBC turnover	↓
Recent transfusion	Increased RBC turnover	↓
Hemodialysis	Shorter RBC lifespan	↓
Metabolic acidosis	Carbamylation of hemoglobin	↑

CONCLUSION

The study conducted observed the prescribing pattern of OHA, Prevalence of comorbidities, Dose adjustment and Glycemic target in geriatric type 2 diabetes mellitus. Study showed that both men and women are at high risk of T2DM.

Metformin was the mostly prescribed OHA both in monotherapy and combination therapy. Prescription trend was moving towards combination therapy especially two-drug therapy.

Hypertension was the most common comorbidity. In the patients having comorbities diabetes related comorbidities had a higher prevalence rate than non-diabetes related comorbidities. The predominance of hypertension and cardiovascular diseases may be due to the fact that Diabetes Mellitus is a risk factor of Atherosclerosis and hypertension.

Dose adjustment is needed for most of the patients with low eGFR and more than half of the patients had controlled glycemic level.

Diabetes management in older adults requires careful assessment of clinical, functional,and psychosocial factors. Before developing glycemic goals and a treatment strategy,eachpatients overall health, coexisting medical conditions,personal preference,coping capacity and factors affecting quality of life should be considered.

Geriatric diabetics need drug dosage adjustment. There are several things to consider when planning treatment for diabetes in older adults. The physiology of diabetes in these patients involves impairment of basal glucose control, reduced prandial insulin secretion, and insulin resistance. Older adults are also at increased risk for

hypoglycemia, so careful attention must be paid to minimize this risk.

REFERENCES

1. American Diabetes Association. Older Adults. Sec 12 in Standards of medical care in Diabetes -2020. Diabetes Care, 2020; 43(Suppl. 1): S157.
2. Struijs JN, Baan CA, Schellevis FG, Westert GP, van den Bos GA. Comorbidity in patients with diabetes mellitus: impact on medical health care utilization. BMC Health Serv Res., 2006 Jul4; 6: 84.
3. Odegard P S, Setter S M, Neumiller J J, Considerations for pharmacological treatment of diabetes in older adults. Diabetes Spectrum, 2007; 20(5): 239-47.
4. Caughey GE, Roughead EE, Vitry AI, McDermott RA, Shakib S, Gilbert AL. Comorbidity in the elderly with diabetes: Identification of areas of potential treatment conflicts. Diabetes. Res. Clin. Pract, 2010 Mar; 87(3): 385-93.
5. Shastry R, Adhikari P, Kamath A, Chowta M, Ullal S, Pai MR. Do geriatrics require dose titration for antidiabetic agents? J Postgrad Med, 2013 Oct-Dec; 59(4): 271-4.
6. Bannister M, Berlanga J. Effective Utilization of Oral Hypoglycemic Agents to achieve Individualised HbA1c targets in Patients with Type 2 Diabetes Mellitus. Diabetes Ther, 2016 Sep; 7(3): 387-99.
7. Leung E, Wongrakpanich S, Munshi MN. Diabetes Management in the Elderly. Diabetes. Spectr, 2018; 31(3): 245-53.
8. Guidoni CM, Borges AP, Freitas OD, Pereira LR. Prescription patterns for diabetes mellitus and therapeutic implication: a population-based analysis, Arq Bras Endocrinol. Metabol, 2012; 56(2): 120-6.
9. Patel B, Bhavit Oza, Patel K, Malhotra S, Patel V. Pattern of Antidiabetic Drugs use in type-2 Diabetic Patients in a Medicine Outpatient Clinic of a Tertiary Care Teaching Hospital. Int. J. Basic. Clin. Pharmacol, 2013- June 2; 2(4): 485-91.
10. Agarwal AA, Jadhav PR, Deshmukh YA. Prescribing pattern and efficacy of anti-diabetic drugs in maintaining optimal glycemic levels in diabetic patients. J. Basic. Clin. Pharm, 2014 Jun; 5(3): 79-83.
11. Valencia WM, Florez H. Pharmacological treatment of diabetes in older people. Diabetes. Obes. Metab., 2014 Dec; 16(12): 1192-203.
12. Kezerly L, Shalew L, Barski L. Treating the elderly diabetic patient: special consideration, 2014; 7: 391-400. Chentli F, Azzoug S, Mahgoun S. Diabetes mellitus in elderly. Indian. J. Endocrinol. Metab. 2015 Nov-Dec; 19(6): 744-52.
13. LeRoith D, Biessels GJ, Braithwaite SS, Casanueva FF, Draznin B, Halter JB. Treatment of diabetes in older adults: An endocrine society Clinical Practise Guidelines. J. Cli. Endocrino. Metab, 2019; 104(5): 1520-74.
14. https://www.mims.com/philippines/drug/info/galvus met/dosage.
15. Dabhi AS, Bhatt NR, Shah MJ. Voglibose: an alpha glucosidase inhibitor. J. Clin. Diagnostic. Res., 2013 Dec; 7(12): 3023-7.
16. Chu WM, Ho HE, Huang KH, Tsan YT, Liou YS, Wang YH.et.al. The prescribing trend of oral antidiabetic agents for type 2 diabetes in Taiwan: An 8-year population-based study. Medicine (Baltimore), 2017 Oct; 96(43).
17. Ioannidis I. Diabetes treatment in patients with renal disease: Is the landscape clear enough?. World. J. Diabetes. 2014; 5(5): 651-58.
18. Munshi M. Managing the "geriatric syndrome" in patients with type 2 diabetes. Consult Pharm, 2008 Apr; 23 Suppl B: 12-6.
19. American Diabetes Association. Classification and diagnosis of diabetes. Sec 2 in Standards of Medical care in Diabetes-2018. Diabetes care, 2018; 41(Suppl. 1): S13-S27.
20. American Diabetes Association Glycemic targets. Sec. 6 in Standards of Medical Care in Diabetes. Diabetes Care, 2018; 41(Suppl. 1): S55–S64.
21.