

Original Article

A STUDY ON DRUG UTILIZATION EVALUATION AND POTENTIAL DRUG RELATED PROBLEMS IN TYPE-2 DIABETES MELLITUS PATIENTS WITH CO-MORBIDITIES IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: The objective of this study is to evaluate prescribing pattern, analyze drug-related problems, identify co-morbidities and complications in Type 2 Diabetes Mellitus patients and also to perform cost analysis of Biguanides, Sulfonylureas, Dipeptidyl Peptidase Inhibitors

Methods: A Prospective observational study was done in General Medicine and Endocrinology Departments of PSG Hospitals. A total of 200 study subjects, including both inpatients and outpatients, above 18 y of age, prescribed with OHAs (Biguanides, Sulfonylureas and DPP4 inhibitors) were included in the study.

Results: Diabetes was more prevalent among males. OHAs were most prescribed in the age group of 51-60 y. Hypertension (71%) was the most common comorbidity and Diabetic neuropathy (23%) was the most common complication found in the patients. Multidrug therapy (72.5%) was most prescribed in diabetic patients, followed by Biguanides. Hypoglycemia was the most prevalent ADR. Cost analysis showed that T. Linagliptin was of high cost and T. Glimepiride being the low cost. Using WHO core indicators prescribing patterns were assessed. Feedback was collected and results were reported to the physicians which showed rational utilization of drugs.

Conclusion: The study on drug utilization conducted in a tertiary care hospital helped us to find out that prescribing trends seems to be progressing towards combination therapy, predominantly two-drug therapy

Keywords: Antidiabetic drugs, Drug utilization evaluation, Naranjo adverse drug reaction scale, WHO core indicators, Prescribing patterns

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INTRODUCTION

The term Diabetes describes a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrates, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both [1, 2].

Diabetes mellitus is a leading cause of morbidity and mortality because of its associated complications viz: Neuropathy, Nephropathy, Retinopathy, and cardiovascular disorders. The prevalence of type 2 Diabetes has been increasing worldwide as a result of excess body weight and physical inactivity.

According to 2019 International Diabetes Federation survey of India, among 997 million population, 88 million (8.8%) people were reported to have Type 2 Diabetes Mellitus [3]. Indians are more prone to diabetes because of obesity and change in lifestyle pattern. The symptoms of Type-2 diabetes are similar to Type-1 diabetes but are often less marked. Consequently, the disease may be diagnosed several years after onset, once complications have become apparent. The lack of compliance towards diabetes could lead to chronic complications, including macrovascular and microvascular [4]. Most of the diabetic patients have relatively poor glycaemic control and are presented with multiple co-morbidities like Hypertension, Dyslipidemia, Coronary artery disease, etc.

Diabetes Mellitus mainly occurs in the older age group though incidence is now increasing in younger population [5]. As elderly diabetic patients have more co-morbid conditions and complications, they are prescribed with multidrug regimen making them more prone to drug-related problems (DRPs). Therefore polypharmacy should be monitored among patients with diabetes as it increases the probability of adverse drug events, drug-drug interactions, which escalates the drug costs and health care costs leading to poor compliance to

medications. Administrative databases seem to be useful in analyzing trends in the prescribing pattern and cost analysis.

Hence the drug utilization evaluation (DUE) studies have become one of the potential tools in the evaluation of the health system and it also suggests modifications in the current prescribing practices to the prescribers to encourage rational use of drugs. Therefore, this study focuses on evaluating the prescribing pattern, analyzing drug related problems, identifying co-morbidities and complications in Type 2 Diabetes Mellitus patients and also performing cost analysis of Biguanides, Sulphonylureas, Dipeptidyl peptidase-4 inhibitors which is one of the components of the Drug utilization metrics

MATERIALS AND METHODS

Study site

The study was conducted at PSG Hospitals, Peelamedu, Coimbatore.

Study approval

This study was approved by the Institution Human Ethics Committee (IHEC, PSG IMSR) of the hospital. The protocol was approved on 08/02/2019, Proposal number: 19/033.

Study design

A prospective observational Drug Utilization Evaluation study.

Study period

The study was conducted for a period of 6 mo.

Study subjects

All T2DM patients who were attending Endocrinology and General Medicine departments with co-morbidities were included in this

study. Patients of either gender who were above 18 y of age and prescribed with Biguanides, Sulphonylureas, DPP4 Inhibitors for Type 2 Diabetes Mellitus were included. Diabetic patients who were pregnant, lactating, patients taking Insulin analogues and those who were not willing to participate in this study were excluded.

Data collection

Patients were approached in the respected departments based on the inclusion and exclusion criteria. After explaining about the study in a regional language, the consent form was collected from the patients prior to data collection. Data regarding the socio-demographic and clinical characteristics of the patients were obtained through interviews and past medical records. From the drug chart review, current medications along with dosage, frequency, route of

administration and duration of therapy have been recorded and assessed for drug interactions, adverse drug reactions, polypharmacy, prescribing patterns and also for cost analysis.

Statistics

The statistical analysis was done using SPSS version 25 and the odds ratio

RESULTS

In this study, a total of 200 patients were included from the departments of Endocrinology and General Medicine of PSG Hospitals, Coimbatore. Both Inpatients and Outpatients were included. Baseline characteristics such as social habits and gender of the patient were summarized in table 1.

Table 1: Baseline characteristics

Characteristics	No of prescriptions	Percentage
Gender		
Male	110	55
Female	90	45
Social habits		
Smoker	55	50
Alcoholic	58	52.7
Both	49	44.5

The age wise distribution of patients with co-morbidities was summarized in fig. 1 in which most prevalent co-morbid conditions were found in the age group of 51-60 y. Diabetic complications were most prevalent in the age group of 51-60 y and patients with a

diabetic history of 5-10 y were more prone to diabetic complications which were summarized in table 2 and table 3. Diabetic complications were observed more in smokers therefore, there is an association between smoking and diabetic complications (p=0.000).

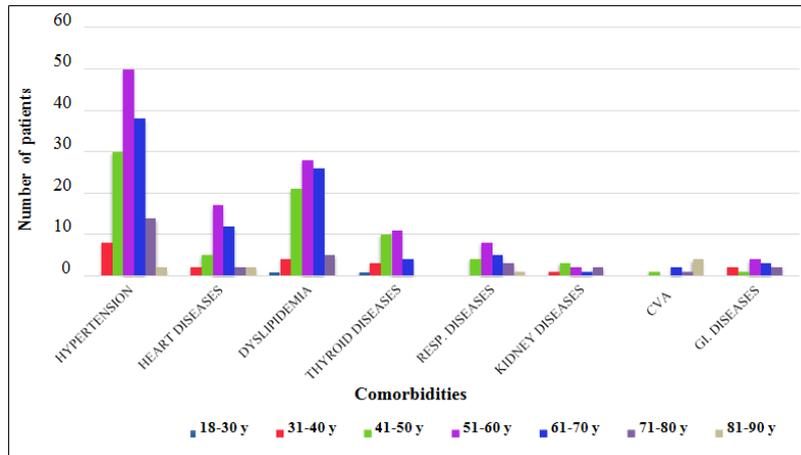


Fig. 1: Age wise distribution of patients with co-morbidities

Table 2: Age wise distribution of patients with diabetic complications

Age group	18-30y	31-40y	41-50y	51-60y	61-70y	71-80y	81-90y
Retinopathy	0	1	4	12	10	2	0
Neuropathy	0	3	14	14	10	5	0
Nephropathy	0	0	2	3	1	1	0
Foot Ulcer	0	2	3	1	0	1	0
Total	0	6	23	30	21	9	0

Table 3: Diabetic duration wise distribution of complications

Diabetic duration	Complications	Percentage
<5 y	18	26
5-10years	34	49
11-15years	12	17.3
16-20years	4	5.7
>20years	1	1.4

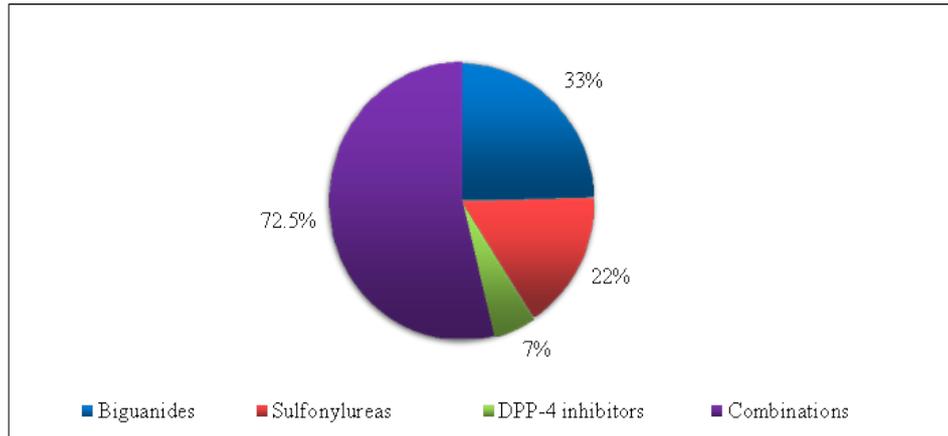


Fig. 2: Drug class wise distribution of OHAs, The drug classes included in this study were Biguanides, Sulfonyl ureas and DPP4 Inhibitors which were summarized in fig. 2

Table 4: Age wise distribution

Age group	Biguanides	Sulfonyl ureas	DPP-4 inhibitors	Combination	
				S. U+BG	DPP4+BG
18-30	0	0	0	1	0
31-40	4	3	0	9	3
41-50	25	12	4	31	8
51-60	34	8	0	46	19
61-70	26	11	2	37	7
71-80	5	2	5	9	1
81-90	1	0	0	2	0
Total (n)	95	36	11	135	38
Percentage (%)	47.5	18	5.5	67.5	19%

Biguanides were more prescribed in the age group of 51-60 y (n=34, 17%); Sulfonylureas in the age group of 41-50 y (n=12, 6%) and its combination in the age group of 51-60 y (n=46, 23%); DPP-4 Inhibitors in the age group of 71-80 y (n=5, 2.5%) and its combination in the age group of 51-60 y (n=19, 9.5%) which are illustrated in table 4.

According to dose wise distribution, the most prescribed doses among the OHAs were:

Biguanides-Metformin 500 mg (n=51, 25.5%); Sulfonyl ureas-Glimepiride 1 mg (n=6, 3%) and Gliclazide 40 mg (n=6, 3%); DPP4 Inhibitors-Sitagliptin 25 mg (n=3, 1.5%); Sulfonyl ureas

Combination-Glimepiride+Metformin 0.5/500 mg (n=22, 11%); DPP4 Inhibitors Combination-Vildagliptin+Metformin 50/500 mg (n=16, 8%).

Fig. 3 shows the distribution of the number of Oral Hypoglycemics prescribed among patients according to their diabetic history in years.

Out of 200 prescription encounters, Biguanides had 69 plain, 10 Extended-Release and 12 Sustained Release preparations, Sulfonylureas had 7 plain and 2 Extended-Release preparations and its combination had 1 plain and 1 Extended Release, DPP4 Inhibitors and its combination had only plain formulation.

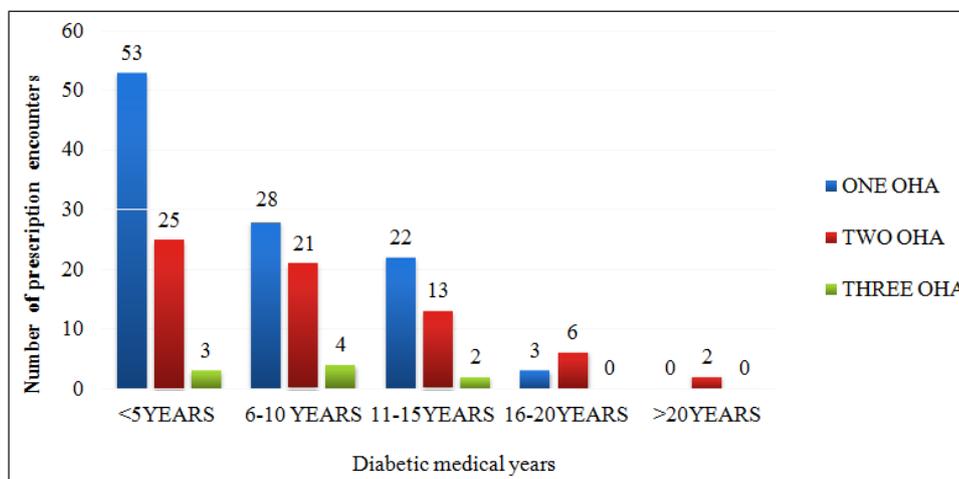


Fig. 3: Distribution of OHAs according to diabetic duration

Distribution of OHAs according to diabetic duration was summarized by fig. 3.

Out of 200 prescriptions, polypharmacy was seen in 35 (17.5%) prescriptions, hyperpolypharmacy in 16 (8%) prescriptions and it was high in patients with the age group of 51-60 y.

Micromedex and Medscape were used to assess drug-drug interaction based on its severity and significance. In this study 72 patients had drug interactions in which 17 were minor, 31 were

moderate and 28 were major which were clinically significant. As more drugs were prescribed in a prescription, more drug interactions were encountered. So, there was an association between Polypharmacy and DI ($p=0.000$).

Out of 200 Diabetic patients, 15 developed ADR in which 10 were caused by Metformin, which shows that there is an association between drug use and ADR ($p=0.017$); table 5 depicts the Adverse Drug Reaction assessed by using Naranjo's scale.

Table 5: Adverse drug reaction

ADR assessment by naranjo algorithm				
S. No.	Suspected drug	Reaction observed	Causality assessment (Naranjo scale)	No of patients
1	Glimepiride	weight gain	Probable	1
2	Glimepiride	weight gain	Possible	2
3	Metformin	hypoglycemia	Probable	3
4	Metformin	hypoglycemia	Possible	5
5	Metformin	GI disturbance	Possible	1
6	Metformin	Dyspepsia	Definite	2
7	Vildagliptin	burning sensation in feet	Possible	1

The prescriptions were analyzed for WHO core indicators in table 6

Table 6: Prescribing pattern

Prescribing Indicators	Total drugs/Encounters	Average percentage (%)	WHO ideal values
Average number of drugs per encounter	997	4.98	1.6-1.8
Percentage of drugs prescribed by Generic Name	79	7.92	20.0-26.8%
Percentage of drug encounters with Antibiotics	33	3.3	13.4-24.1%
Percentage of drug encounters with Injections	77	7.7	100%
Percentage of drugs prescribed from EML/Formulary	997	100	100%

Cost analysis was done for the selected classes of OHAs which showed that combination of DPP-4 Inhibitors (Teneligliptin+Metformin) was cheaper when compared to other prescribed brands of DPP-4

Inhibitors (Sitagliptin). It was also found that the most expensive brands of DPP-4 Inhibitors (Linagliptin) was less prescribed. Metformin was the most prescribed brand and also one of the cheapest drugs among OHAs. Cost analysis showed that among Sulphonylureas, Glimepiride was the cheapest, but more often, Sulphonylureas and Biguanide combinations (Glimepiride+Metformin) were prescribed with reasonable prices.

DISCUSSION

In this study, the prevalence of T2DM were more in males 110 (55%) compared to females 90 (45%), which was in contrast to the previous study in which the prevalence of T2DM were more in females when compared to males [6]. Hypertension (71%) and Dyslipidemia (42.5%) were the most prevalent comorbid conditions in the age group of 51-60 y. This was similar to the study conducted in 2017 in which hypertension was the most common comorbidity observed [7, 8]. Patients with diabetic duration of 5-10 y showed a significant effect on the prevalence of Diabetic neuropathy. In this study the association between duration of diabetes and risk of neuropathy is strong which was in concordance to the previous study in which diabetic neuropathy is present mainly in patients after 5 y of diabetes history [9,10]. Multidrug Therapy (72.5%) was most prescribed among the OHAs followed by Biguanides (33%). The most prevalent multidrug therapy was a two-drug combination Glimepiride+Metformin (45.5%). This was similar to the previous study in which two-drug therapy-Glimepiride+Metformin was most prescribed [11]. During this study, 15 ADRs (7.5%) were recorded in which the most common were hypoglycaemia (n=8), dyspepsia (n=2) and GI disturbances (n=1). This was in concordance with the previous study in which hypoglycaemia was the most common ADR found [12, 13].

Polypharmacy (17.5%) and Hyperpolypharmacy (8%) were observed. The maximum level of polypharmacy was observed in the

age group of 51-60 y followed by patients with the age group of 61-70 y and 41-50 y. This was in contrast to the previous study in which the level of polypharmacy increased with age of patients [13]. The Prescribing patterns were evaluated using WHO Core Indicators. The average number of drugs per prescription was 4.98%, which was higher when compared to WHO Ideal Value (1.6-1.8%), showing high degree of polypharmacy. Similarly, the average number of drugs per prescription was also higher than the findings of the studies conducted in Ayder Referral Hospital of Northern Ethiopia: 2.61 [14]. Percentage of drugs prescribed by generic name (7.92%) was lesser than WHO ideal values (100%), which shows less tendency of the prescribers to prescribe drugs by generic names. Percentage of injection and antibiotics were 7.7% and 3.3%, respectively, which was lesser when compared with WHO Ideal Values. This showed less tendency of over usage and prescribing expensive drugs. However, the percentage of injection and antibiotics were lower when compared to other reports from studies conducted in Northern Ethiopia [15]. The percentage of drugs prescribed from EML/Formulary was found to be 100%, this shows prescribing was based on national essential drug/formulary. Among the prescribed brands, DPP4 Inhibitors were of high cost and Biguanides were found to be cheaper. Cost analysis also showed that Sulphonyl urea-Biguanide combinations and Biguanides were the most prescribed and economical. This was in concordance with the previous study in which Biguanides and Sulfonyl urea-Biguanide combination were most prescribed. Both of these therapies were economical and DPP-4 Inhibitors were costlier [16]. The limitation of the study was the synthesis of data sources regarding pharmaco-economic evaluation was impossible due to the shorter duration of the study.

CONCLUSION

This study helped us to find out the current prescribing patterns of oral antidiabetic drugs in Type 2 Diabetes Mellitus patients. The prescribing trends seems to be progressing towards combination therapy predominantly two-drug therapy. Economic burden should not affect the treatment regimen of the patient therefore it is the physician's responsibility to be aware of the inter-brand price

variations and to prescribe drugs of cheaper prices. Rational drug use is a significant factor to be checked for the ideal benefit of drug therapy inpatient care.

AUTHORS CONTRIBUTIONS

Conceived and designed the study: Prudence. A. Rodrigues, Naresh Kumar. M, Dawn Teslin Damien, Mary Cecil. K. T and Reshma. S. S. Performed the study: Naresh Kumar. M, Dawn Teslin Damien, Mary Cecil. K. T and Reshma. S. S. Contributed materials/analysis tool: Prudence. A. Rodrigues. Manuscript preparation and correction and Correspondence: Dawn Teslin Damien, Mary Cecil. K. T and Reshma. S. S. Peer support: Susan Varghese Paul.

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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