

Asian Journal of Pharmaceutical Education and Research

Vol -4, Issue-2, April-June 2015

ISSN: 2278-7496

## **RESEARCH ARTICLE**

# ASSESSMENT OF ANTI- HYPERGLYCAEMIC DRUG PRESCRIPTION PATTERN: A PROSPECTIVE, PHARMACOEPIDEMIOLOGIC STUDY

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Accepted on 23 March 2015

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## Abstract:

Diabetes mellitus is a chronic illness associated with significant morbidity and mortality. Diabetes treatment depends on the type and severity of the diabetes. prospective observational study, in the general medicine department of a tertiary care hospital. Ethical clearance was obtained prior to the study. Patient data was collected by using a patient data collection form and their drug use was recorded and subjected to analysis. A total of 472 patient's data was recorded and analyzed for the prescription pattern of anti-diabetics using WHO Core Indicators. 67.37% prescriptions contained a single anti-diabetic drug whereas 32.62% prescriptions a combination of anti-diabetic drugs. Drugs were classified according to their class where metformin(41.19%) was found to be most prescribed followed by sulphonylureas. The combination therapy, Glimepiride + Metformin combination was most frequently prescribed followed by Glimipride+ Insulin. Average number of drugs per prescription was 5.5±2.9. Drugs prescribed by generic names(98.26%) was very much higher than prescribed by their brand names(1.73%).

**Key Words:** Diabetes mellitus; Anti-hyperglycaemic drug Prescribing Pattern, Drug utilization studies, ATC code.

#### **INTRODUCTION:**

Drug utilization research was defined by WHO as the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting in medical and socioeconomic consequences. Drug utilization studies are the actual powerful exploratory tools to ascertain the role of drugs in the society.<sup>[1]</sup> It aims to analyse the present state and the development of drug usage at various levels of the healthcare systems whether national, local or institutional.<sup>1</sup>

Prescription is a written order by a registered medical practitioner to a pharmacist to compound, manufacture ,dispense a medication to the patient. Irrational prescription of drug has become very common in clinical practice due to lack of knowledge about drugs and also unethical drug promotion.<sup>2</sup> Irrational use of drugs can lead to misuse, underuse or overuse of medicines.<sup>3</sup>Hence EML (essential medicine list) was formulated to promote rational prescribing. There is a dire need of rational drug use, still there is a lack of pioneer drug utilization studies in this field.

In India, treatment of type 2 diabetes starts with changing lifestyle and dietary measures which are usually the first step, the second being pharmacotherapy. In the early 1990s in India, as in the rest of the world, there were three groups of oral blood glucose-lowering drugs available, i.e. biguanides, sulphonylureas and  $\alpha$ -glucosidase-inhibitors. After 1999, groups of drugs, i.e. Meglitinides (Repaglinide, Nateglinide) and two new Thiazolidinediones (Rosiglitazone, Pioglitazone) became available. Due to the availability of multiple classes and multiple drugs in each class it becomes necessary for the physician to prescribe the oral hypoglycaemic compound which is most beneficial to the patient. A study of factors(patient factors like age, sex, BMI and coexisting illnesses determine the prescription) affecting prescribing of a particular drug and a combination of drugs gives a clear view as to how a particular drug or combination of drugs control a disease in different patients. Many international and national guidelines provide evidence-based recommendations for the treatment of diabetes. It is recognized that new guidelines or insights are not always implemented in daily practice because there are many individual patient factors which need to be considered while prescribing any drug.<sup>4</sup>

Diabetes mellitus (DM) is a chronic metabolic disorder and it has chronic long term and short term complications and is a disease which has high morbidity and mortality rates. Patients with type 2 diabetes are at an increased risk for diseases and treatment related

complications. This is particularly true at a point where patients are switched from oral monotherapy, to combination drug therapies. The recent guideline of the German Diabetes Society (Deutsche Diabetes Gesellschaft DDG) recommends to combine metformin with a number of different oral antidiabetic drugs or a GLP-1 analogue in patients whose HbA1c remains  $\geq 6.5\%$  but is < 7.5% after 3-6 month of metformin monotherapy treatment (with nutritional counselling and sports). Insulin should be added if HbA1c is still  $\geq 6.5\%$  after 3-6 month treatment with combination therapy or if HbA1c is  $\geq 7.5\%$  after the initial metformin/other oral anti diabetic monotherapy. Drug therapy is the most commonly used method of any disease treatment in general practice. However, the patterns of drug prescribing are often inappropriate.<sup>5</sup>

## **OBJECTIVE:**

The objective of this study was to assess the pattern of anti-hyperglycemic drug prescription pattern and usage among the diabetes patients attending general medicine department in a tertiary care teaching hospital in south India.

## MATERIALS AND METHODS:

**Study design:** This is a prospective, observational, non-interventional, uncontrolled, unicentric, pharmacoepidemiologic study.

**Data collection:** The patient data was collected by using a patient data collection form and their prescription pattern and drug use was recorded and subjected to analysis.

**Study duration:** The study is conducted for a period of 6 months i.e.; from april 2014 to September 2014 in the general medicine (both inpatient and outpatient) department.

**Study site:** Government General Hospital, Guntur is a 1200 bedded tertiary care teaching hospital with 24 medical departments, one among them being general medicine department.

**Significance of the study:** There were no studies conducted previously in this hospital regarding the pattern of drug use in diabetes mellitus. Hence the present study is taken to know the pattern of drug use in diabetes mellitus. This type of study will help to provide data which might be helpful in improving rational prescribing.

## Selection criteria:

## Inclusion criteria:

Patients of the age group 30 years and above, of both the genders – male and female, diagnosed with both of either type -1 Diabetes mellitus, or type -2 Diabetes mellitus attending the general medicine department of Government General Hospital, Guntur hospital were included.

## **Exclusion criteria:**

Patients with gestational diabetes, Patients with any chronic psychiatric illness, Patients admitted in wards other than general medicine department, Patients with serious illness or who are critically ill and transferred from general medicine department to acute medical care unit or intensive care unit were excluded from the study. Patients who are pregnant, and/or breast feeding their infants were also excluded from the study.

## STATISTICAL ANALYSIS:

The data was subjected to descriptive analysis using Microsoft Excel. Drugs were classified according to the WHO ATC classification<sup>6</sup> and verified by WHO EML <sup>7</sup> (Essential Medicine List) as well as NLEM <sup>8</sup> (National List of Essential Medicines) 2011. Different parameters were given as percentage and analyzed using simple statistical tests.

## **RESULTS AND DISCUSSION:**

Data from 472 diabetic patient records were analysed. Out of 472 patients, 223 were male patients and 249 were female patients. Female preponderance was seen in our study, which is similar to the findings of M A Kumar, A Nazir, K Shailaja et al <sup>9</sup>,a study conducted in type-2 diabetic patints in 2011 in Tamil Nadu. But, male preponderance was seen in a study conducted in Indore in India<sup>10</sup>,whereas nearly almost equal numbers of male and female was reported in a study done by Acharya KG et al in 2013<sup>11</sup>.

Among 472 diabetic patints, most of the patients were in the age group of 51-60 both for males (48.43%) and for females(40.9%) as depicted in table -1.

Age in Years	No. of Males(%)	No. of Females(%)
30-40	0 (0 %)	1(0.4%)
41-50	6(2.6%)	9(3.61%)
51-60	108(48.43%)	102(40.9%)
61-70	63(28.25%)	81(32.5%)
71-80	39(17.48%)	52(20.8%)
>80	7(3.13%)	4(1.6%)
Total	223 (47%)	249 (53%)

Table -1: Age wise distribution among diabetes patients.

Hypertension (81.7%) was the most common comorbid condition followed by coronary artery disease(61.4%) in our study. These results are similar to the findings of other studies done on diabetic population.<sup>11,12</sup> The most common comorbid conditions, besides

hypertension and coronary artery disease, include Ischaemic stroke, Haemorrhagic stroke, Anaemia. Chronic Renal Failure(CRF) Tuberculosis(TB), Asthma, Angina pectoris, hyperthyroidism, alcoholic liver disease, cirrhosis of liver, malaria, dengue fever, Chronic Obstructive Pulmonary Disease(COPD), Myocardial Infarction (MI), Urinary Tract Infection(UTI), Acute Renal Failure(ARF), peptic ulcer, inflammatory bowel disease, squint orbit, obesity, gastro oesophageal reflux disease, congestive cardiac failure, cerebral palsy, migraine, glaucoma, rheumatoid arthritis, polyarthritis. Diabetic neuropathy, Diabetic nephropathy, Diabetic retinopathy and diabetic foot were the complications which were also found to be prevalent among the patients. Family history of diabetes mellitus was reported by 59% of patients which is in accordance with a study done by Acharya KG et al in 2013<sup>11</sup>.

Metformin (A10BA02 =31.72%) was the most commonly prescribed antidiabetic agent followed by glimepiride(A10BB12=18.6%). These findings are also similar to a study done by Acharya KG et al in 2013<sup>11</sup>. The results of our findings were as depicted in figure-2.

The antidiabetic drug utilization in diabetes patients according to WHO-ATC coding system<sup>13,14</sup> has been shown in table-2.

Pharmacological class	Name of drug	WHO- ATC code	No. (as %) of
of the drug (ATC code)		of individual drug	patients
Biguanides (A10BA)	Metformin	A10BA02	131 (41.19%)
Sulphonylureas	Glimepiride	A10BB12	92 (28.93%)
(A10BB)	Glibenclamide	A10BB01	78 (24.52%)
Thiazolidinediones (A10BG)	Pioglitazone	A10BG03	01 (0.31%)
Insulin (A10A)	Human insulin (Short acting)	A10AB01	10 (3.14%)
	Pre mixed insulin (human mixtard)	A10AD30	15 (4.71%)
	Long acting insulin(detemir)	A10AE30	01 (0.31%)

Table-2: Utilization of antidiabetic drugs in diabetes patients.

## Analysis of prescription pattern of anti-hyperglycaemic drugs:

No. of prescriptions containing a single anti-diabetic drug = 318The % of prescriptions containing a single anti-diabetic drug =  $318/472 \times 100 = 67.37\%$ 

No. of prescriptions containing an oral (single) anti-diabetic drug= 292

The % of prescriptions containing an oral (single) anti-diabetic drug= $292/472 \times 100 = 61.86\%$ No. of prescriptions containing parenteral (single) anti-diabetic drug = 26

The % of prescriptions containing parenteral (single) anti-diabetic drug= $26/472 \times 100$  = 5.50%

No. of prescriptions containing a combination (more than a single) of anti-diabetic drugs =154

The % of prescriptions containing a combination (more than a single drug) of anti-diabetic drugs =  $154/472 \times 100 = 32.62\%$ 

The single use i.e., monotherapy was screened and metformin was the most commonly used anti-diabetic drug. Metformin (A10BA02 =41.19%) was the most commonly prescribed antidiabetic drug followed by glimepiride(A10BB12=28.93%) and glibenclamide (A10BB01= 24.52%).

Among combination therapy, Glimepiride + Metformin combination was most frequently prescribed followed by Glimepiride+ Insulin, Insulin+ Metformin , Glimepiride+ Metformin, Insulin+ glibenclamide, and Pioglitazone+Metformin. Hypoglycemia was the most commonly found ADR of hypoglycemic drugs in 10(3.14%) of the diabetic patients. In a nutshell, 318(67.37%) prescriptions contained a single anti-diabetic drug whereas 154(32.62%)prescriptions contained combination of anti-diabetic drugs. The combination used commonly to treat diabetes was Glimipride + Metformin.

To our surprise, Dipeptidyl peptidase-4 inhibitors, alpha glucosidase inhibitors, GLP-1 receptor agonists, first generation sulphonylureas, phenylalanine analogues were not at all prescribed to even a single patient because of the lack of availability and to be purchased from outside the vicinity of the hospital, whereas all the remaining drugs prescribed here are easily available that too at free of cost to all the patients attending the hospital for treatment.

Regarding adjuvant drug utilization therapy, ceftriaxone was the most commonly used drug followed by pantoprazole. Either of pantoprazole or ranitidine had a place in almost all of the prescriptions.ACE inhibitors, thiazide and loop diuretics, beta blockers, calcium channel

blockers, aspirin, clopidogrel, atorvastatin, multivitamin supplements and other drugs were also prescribed to the patients because of existing comorbid conditions.

Drug interactions with the anti diabetic drugs were screened with the help of online resources such as Micromedex, Clinical Pharmacology data bases and some standard text books. Drug interactions of Insulin with levofloxacin, metoprolol and atenolol was observed.

A total of 17 drug interactions were recorded out of which the most common drug interaction was found between Insulin with levofloxacin tablets which causes either hyperglycemia or hypo glycemia in 4 prescribed patients. Insulin with atenolol drug interactions was found in 3 patients, which cause either hyperglycemia or hypo glycemia. Metformin with enalapril was observed in 2 patients, which may cause hyperkalaemic lactic acidosis, Insulin with norfloxacin in 2 patients which may cause hyperglycemia / hypoglycemia. Insulin+ aspirin were observed in 2 patients which may cause hypoglycemia. Out of the total 472 prescriptions studied, WHO core indicators were assessed and are explained as in the table-3.

WHO core indicators	Results
Total number of drugs	2598
Total antidiabetic drugs	919 (35.37%)
Total number of drugs per prescription	5.5(2593/472)
Total number of anti-diabetic drugs per prescription	1.6(919/472)
Drugs on WHO EML	1876 (72.20%)
Drugs on NLEM 2011	1991 (76.63%)
Drugs prescribed by brand name	45/2598 (1.73%)
Drugs prescribed by generic name	2553/2598 (98.26%)
Total encounters having injectable formulation	72/2598 (2.77%)
Drugs prescribed as fixed dose combinations	38/2598 (1.46%)

	Table-3:	Elaborates	the	WHO	core indicators.
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The average number of drugs per prescription was 5.5(2593/472) which shows polypharmacy and can lead to potential drug-drug interactions. Drugs on WHO EML<sup>[7]</sup> were

1876 (72.20%) while on NLEM <sup>[8]</sup>were 1991(76.63%) which is almost same which is similar to a study done in which the drugs from essential drug list were 48.21%.<sup>[9]</sup>

Drugs prescribed by generic names were 2553/2598 (98.26%)which is very much higher than that prescribed by their brand names 45/2598 (1.73%) as illustrated in figure-2 which is the need of the hour for physicians as well as patients or medicine consumers to opt for generic drug usage or utilization of pharmaceuticals and medicines in order to reduce economical burden on the society as well as the consumers or patients.

## **CONCLUSION:**

The information gathered should be a pointer to the trends in prescribing patterns. The present study could serve as a frame work upon which further studies in prescription audit can be launched to investigate the scope for educational intervention and improvement in prescribing patterns. The study emphasizes both needs and feasibility to perform prescription audit analysis using the accepted method of monitoring the utilization of drug in Indian setup. But still certain aspects like using fixed dose combinations during initiation of treatment, providing life style modification, changing the prescription with different combinations and doses of anti diabetic drugs in order to attain normal blood glucose levels, providing advice on life style modification, were to be addressed as per guidelines. Medical audit improves the standards of treatment at all levels of health care delivery system. The study of prescribing pattern is a component of medical audit which seeks monitoring, advice, evaluation and necessary modifications in the prescribing practices of the prescribers to achieve rational and cost effective medical care. It is necessary to define prescribing pattern and to identify the irrational prescribing habits to drive a remedial message to the prescribers.

Besides the above, the report suggests that there is a need of hospital formulary and incorporating more drugs as per the formulary committee recommendations. Eventually, it will be a model itself on the national and WHO essential medicine list, which may promote the rational use of medicines and ultimately, the quality of patient care.

**Acknowledgements:** The authors would like to thank Prof. N.Rama Rao, Principal, Chalapathi Institute of Pharmaceutical Sciences, Guntur, A.P, India and all the teaching staff of Chalapathi Institute of Pharmaceutical Sciences, for their valuable support throughout the study.

## Source of Support: Nil.

Funding: Not applicable

Conflicts of Interest: The authors declare that they have no competing interests.

#### LIST OF ABBREVIATIONS:

DM- Diabetes mellitus
BMI- Body Mass Index
ATC- Anatomical Therapeutic Chemical classification of drugs
DDD- Defined daily dose
EML- Essential Medicine List
NLEM- National List of Essential Medicines
OPD- Outpatient Department
WHO- World Health Organization

ADR- Adverse drug reactions.

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