A Study on Prescribing Pattern and Potential Drug-drug Interactions in Type 2 Diabetes Mellitus Inpatients

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ABSTRACT

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Over the last decade, diabetes mellitus has emerged as an important clinical and public health problem throughout the world. The aim of the study is to evaluate prescribing pattern and potential drug-drug interactions in hospitalized patients with type 2 diabetes mellitus. The prospective study was conducted over a period of six months in the department of Medicine, Bharati Hospital. The prevalence of type2 diabetes was high in male 57.14 % than female 42.86%. Majority of the patients 51 (48.57%) belonged to age group of 41–60 years. Average drugs per prescription were 12.2. 99.0% of the drugs were prescribed by their brand names. 73.77% of the drugs prescribed were from the WHO list of essential drugs. Totally, 58.10 % of patients were on monotherapy and human insulin (50.48%) was commonly prescribed. In combination therapy, Glimepride and Metformin with insulin (10.48 %) were mostly consumed followed by Glimepiride and Metformin (4.76%) fixed dose therapy. 60 drug -drug interactions were encountered in the study, comprising of 18 (17.14%) actual and 42 (40.00%) were potential drug -drug interactions. As per severity, 16.67% were major, 72.22% were moderate and 11.11% were minor. The potential drug-drug interactions are frequent in type 2 diabetes mellitus and hence, deserve clinical attention. In our study, the generic drug prescription is low and the essential drug prescription is high, hence the prescription by generics should be promoted more for cost effective treatment.

Keywords: Diabetes Mellitus, potential and actual drug-drug interaction, prescribing pattern.

INTRODUCTION

Diabetes Mellitus is an elevated blood glucose associated with absent or inadequate pancreatic insulin secretion, with or without concurrent impairment of insulin action.[1] According to the

Diabetes atlas published by the International Diabetes Federation (IDF), there is an estimated 40.

Million persons with diabetes in India in 2007 and this number is predicted to rise to almost 70.

Million people in 2025.[2] The study of prescribing pattern is a component of medical audit that does monitoring and evaluation of the prescribing practice of the prescribers as well as recommends necessary modifications to achieve rational and cost-effective medical care and it helps to evaluate and suggest modifications in prescribing practices of medical practitioners so as to make medical care rational.[3] Reviewing prescribing patterns could provide feedback to prescribers and assures quality medical care. This study also attempts to analyze the current prescription patterns of drugs used in the treatment of type 2 diabetes mellitus patients. The

findings of this study are expected to provide relevant and useful feedback to physicians. The diabetes mellitus patients are generally treated with many pharmacological agents. In addition to the blood glucose control, treatment of concurrent illnesses and cardiovascular protective agents generally leads to polypharmacy and the chance to drug related problems in the prescriptions.[4] Drug-drug interaction is among the major drug related problems. A drug interaction is said to occur when the effect of one drug is changed by the presence of another drug, food, or by some environmental chemical agent.[5] A potential drug-drug interaction is an event that is likely to develop if pharmacists do not make any appropriate intervention. Drug-drug interactions pose significant challenge to health care providers and may affect morbidity, mortality and a patient's quality of life. In this present study, we have sought to analyze the prescription trend and the potential drug-drug interactions in type 2 diabetes mellitus patients.

MATERIALS AND METHODS

A prospective observational study was carried out for the duration of six months among the patients under inclusion criteria. All the patients above 18 years of age of either sex and the patients admitted in the medicine ward were included in the study.

For data collection and documentation Patient profile form was designed which includes information on patients demographic details (e.g. Patient's Name, Age, Sex,

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educational status, employment, date of admission and date of discharge), presenting complaints, provisional/confirmed diagnosis, social history, past medical/medication history, current medications, discharge medications, laboratory test reports.

The collected data were analyzed and potential and actual drug-drug interactions were screened by using Micromedex Healthcare Series 2.0.

RESULTS

A total of 105 diabetes mellitus patients were enrolled in the study, out of which 57.14% were males and 42.86% were females. (Fig.1)

Fig. 1: Sex Distribution

Male = 60
Female = 45
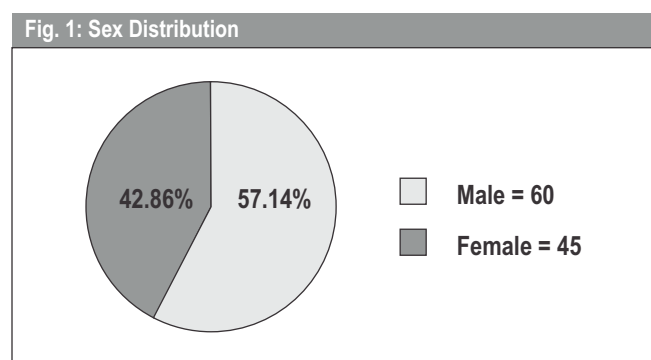
Most patients belong to the age group of 41-60 years (48.57%) followed by > 60 years (44.76%) (Table No.1).

Table 1: Age wise Distribution

Age (in years)	Male (n=60)	Female (n=45)	Percentage
Young group (18–40)	4	3	6.67%
Middle-age group (41–60)	23	28	48.57%
Elderly group (>60)	33	14	44.76%

Out of 105 patients, 88 (83.81 %) patients were found suffering from Concurrent illnesses. Distribution of concurrent illnesses is described (Table No. 2) where Hypertension was the most common co-morbidity present in 24 patients (27.27 %) followed by hypertension with Ischemic heart disease (12.50 %).

Table 2: Distribution of Concurrent illnesses (n=88)

Co-morbidities	No. of Patients	Percentage (%)
Hypertension	24	27.27
Hypertension+ Ischemic heart disease	11	12.50
Hypertension + Coronary artery disease	1	1.14
Chronic renal failure	1	1.14
Ischemic heart disease	1	1.14
Other Co-morbidities	50	56.82

The prescription trend were analyzed, Table no.3 reveals, out of 1281 drugs prescribed to the type 2 diabetes mellitus inpatients, 1271 drugs were prescribed by their brand names. Average number of drugs per prescription was 12.2. Prescriptions for injections and antibiotics were 34.43% and 4.61%, respectively.

Table 3: Prescription details in diabetes mellitus patients

Details of prescription	Number
Total number of prescription analyzed	105
Total number of drugs prescribed	1281
Average number of drugs per prescription	12.2
Number of drugs from WHO essential drug list out of total number of drugs prescribed	945 (73.77%)
Number of drugs prescribed by generic name out of total number of drugs prescribed	10 (0.78%)
Number of encounters with an antibiotic prescribed	59 (4.61%)
Number of injections out of total number of drugs prescribed	441(34.43%)
Total number of anti diabetics out of total number of drugs prescribed	171 (13.35%)

The percentages of patients on anti diabetic monotherapy, combination therapy and fixed dose therapy were 61 (58.10%), 39(37.14 %) and 5 (4.76%) respectively (Fig. 2).

Fig. 2: Anti Diabetics prescription pattern

Monotherapy = 61
Combination = 39
Fixed Dose = 5
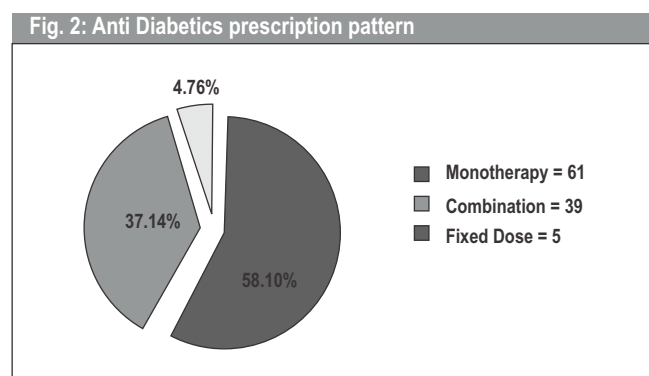
The study revealed that Human insulin preparation was the most commonly prescribed in 53 (50.48%) patients. Among the drug combinations, 11 (10.48%) patients received glimepiride and metformin with human insulin followed by 4 (3.81%), 4 (3.81%) and 5 (4.76%) patients were on metformin with (glimepiride and metformin), human insulin with metformin, human insulin with glipizide, respectively. 5 (4.76%) patients were on a fixed dose combination of oral hypoglycemic agent (metformin + glimepiride) (Table no. 4).

Table 4: Utilization pattern of anti diabetic drugs		
Drugs	**Total Number of prescriptions**	**Percentage (%)**
Monotherapy		
Biguanides		
Metformin	4	3.81
Sulfonylureas		
Glimepiride	1	0.95
Alpha-glucosidase inhibitors		
Voglibose	3	2.86
Insulin	53	50.48
Combination therapy		
Insulin + (Glimepiride + Metformin)	11	10.48
Insulin + Glipizide5	4	4.76
Metformin + Insulin	4	3.81
Metformin + (Glimepride + Metformin)	4	3.81
Insulin + Glimepride	1	0.95
(Glimepiride + Metformin) + Voglibose	1	0.95
Insulin + (Pioglitazone + Glimepiride)	1	0.95
(Glimepiride + Metformin) +(Voglibose+ Metformin)	1	0.95
Insulin+(Metformin+Chromium+Pioglitazone)	1	0.95
Insulin+(Glimepiride+Metformin+pioglitazone)	1	0.95
(Glimepiride + Metformin+ Pioglitazone) + voglibose	1	0.95
Insulin + Metformin + Glipizide	2	1.90
Insulin + (Glimepiride + Metformin) + Sitagliptine	1	0.95
Insulin + (Glimepiride + Metformin) +(Voglibose + Metformin)	1	0.95
Insulin + Metformin + Repaglinide + Sitagliptine	1	0.95
Analogue mixtures + Human insulin + Pioglitazone	1	0.95
(Glimepiride + Metformin) + Metformin + Insulin	1	0.95
Glibenclamide + Metformin + Insulin	1	0.95
Fixed dose combination		
Metformin + Glimepride	5	4.76

The most commonly medication class prescribed were proton pump inhibitors 87 (82.86%) Antiemetics 62 (59.05%), Antihypertensive 60 (57.14%), Antiplatelets 58 (55.24%), nutrient supplements 46 (43.81%) as presented in Fig. 3.
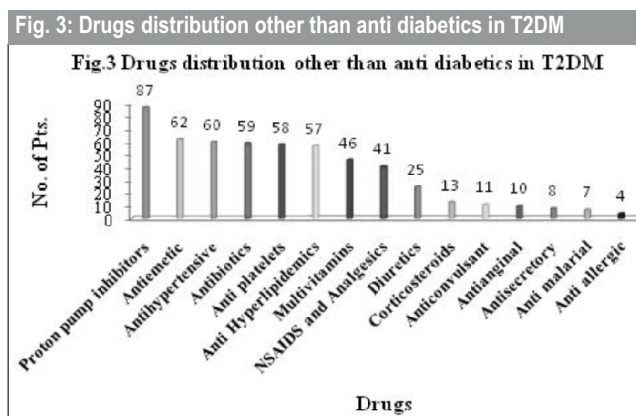
Fig. 3: Drugs distribution other than anti diabetics in T2DM

Sr. No.	No. of Drugs/ Rx	No. of Cases	Potential					Actual				
			Minor	Moderate	Major	Total	Percentage	Minor	Moderate	Major	Total	Percentage
1.	1-5	03	00	00	00	00	00.00	00	00	00	000	0.00
2.	6-10	25	00	09	00	09	21.43	01	03	00	04	22.22
3.	>10	77	00	29	04	33	78.57	01	10	03	14	77.78
Total		105	00	38	04	42	100.00	02	13	03	18	100.00

Table 5: Drug-Drug Interaction

Sr. no.	Interaction	Frequency	Outcomes	Mechanisms
1	Aspirin-Regular Insulin	4	May result in hypoglycemia (CNS depression, seizures).	Pharmacodynamic
2	Carvedilol- Regular Insulin	3	May result in hypoglycemia, hyperglycemia or hypertension.	Pharmacodynamic
3	Atenolol- Regular Insulin	3	May result in hypoglycemia, hyperglycemia or hypertension.	Pharmacodynamic
4	Ciprofloxacin- Regular Insulin	3	May result in changes in blood glucose and increased risk of hypoglycemia or hyperglycemia.	Pharmacodynamic
5	Fenofibrate-Glimepiride	3	May result in an increased risk of hypoglycemia.	Pharmacodynamic

Table 6: Top 5 drug-drug interaction.

DISCUSSION

Diabetes mellitus is one of the major non communicable diseases which are growing very fast in this modern era. The prevalence of Diabetes Mellitus in our study set up was 7.94%. These results are found to be in accordance with the study conducted in Bangalore where the prevalence rate was found to be 4-11.6% in urban dwellers.[6] In our study the prevalence of type2 diabetes was high in males 57.14 %. Males predominated in the study population which is in agreement with the results of various other studies in India[7] and United States.[8]

There was higher prevalence of diabetes mellitus in middle age group, highest being 48.57 % in age group 41-60 years and 44.76 % in above 60 years age group. This higher prevalence in younger age group may be due to the lifestyle of the younger population and also the stress factor which unmasks diabetes causing blood sugar to rise.[9] A total 88 (83.81%) patients suffered from co-morbid condition. Hypertension accounted for 27.27 % of the total complications which was lower than in the study reported in Nepal (Hypertension accounted for 70.62% of the total complication).[10] Our study findings are also similar to the study conducted by Arauz-Pacheco *et al.* in Texas medical center that hypertension is more common complication affecting 20-60% of people with diabetes.[11]

The prescription trend were analyzed, out of 1281 drugs prescribed to the type 2 Diabetes mellitus inpatients, 1271 drugs were prescribed by their brand names. The average number of drugs per prescription is 12.2; this was high when compared to previous records of 2.60, 3.03 and 4.07 from various specialty clinics in India and 2.9 from Hong Kong .[12] The high average number of drugs prescribed to patients with diabetes is not surprising. It is recognized that patients with diabetes mellitus are generally prescribed more drugs than other patients. Prescriptions for Injections and antibiotics were 34.42% and 4.61% respectively. 99.22% of drugs were prescribed by their brand names which is higher and 0.78% were prescribed by their generic names which is lower than study conducted by M Ashok Kumar et al. in tertiary teaching care hospital, Tamilnadu.[13] The average number of drugs per prescription, percentage of drugs from WHO essential drug list and injections were found to be 12.2, 73.77% and 34.43%, respectively which were quite higher whereas the percentage of anti diabetics prescribed was found to be lower than the study conducted by Adibe M.O et al[14], L. sutharson et al.[15] and M.Ashok et al.[13]

The pattern of anti diabetic drug utilization was studied. 58.10% of patients were on monotherapy and 41.90% were on combination therapy for diabetic control which is similar to the study conducted by M Ashok Kumar et al. in tertiary teaching care hospital, Tamilnadu[13] while another study conducted by Kannan et al. in Tamilnadu reveals that monotherapy (2.47%) is lower and combination therapy (56.93%) is higher than our study.[16]

A Drug utilization study is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physician and help to promote rational use of drugs. In patients with type-2 diabetes treatment may be initiated with monotherapy followed by early intervention with a combination of oral agents, including a sulfonylurea/biguanides as a foundation insulin secretagogue in addition to a supplemental insulin sensitizer. In our study insulin as a monotherapy secured highest utilization percentage (50.48%) amongst all anti diabetic drugs. Several studies showed that a combination of sulfonylurea with metformin has been most widely used.[17]The present study also showed that a combination of sulfonylurea and metformin was most frequently prescribed 8.57%. In few patients, failure of oral hypoglycemic allowed to switch over to Insulin preparations. In most patients, the failure of three oral agents used together calls for the use of insulin alone or in addition to an oral agent.

Numerous studies have shown that a combination of insulin and sulfonylurea is more effective than insulin alone in the treatment of patients with type 2 diabetes mellitus after secondary failure to oral drugs, leading to better glucose profiles and/or decreased insulin needs. The present study also showed that a combination of insulin and sulfonylurea plus metformin was most frequently prescribed 18.10% which is comparatively lower than the study conducted by ARSHAD et al. where he reported 57.09%.[16] Metformin does not promote weight gain and has beneficial effects on several cardio vascular risk factors. Accordingly, metformin is widely regarded as the first drug of choice for most patients with type-2 diabetes mellitus .Our study also supports the same 30.47 % received metformin combination with other oral antidiabetic drugs/insulin preparations.

In this study among the second generation sulfonylureas, glimepiride was most commonly prescribed. Adding a second agent is usually better than increasing the dosage of an agent that has already been given in a nearly maximum dosage. In some patients three drug combinations may be useful.[18] In this study, 29.52 % patients received two drugs which is higher, 6.67% patients received three drug and 0.95% patients received four drug combination of anti diabetics which are lower as compared to the study conducted by Kannan et al.[16] Drugs from the alimentary tract and metabolism constituted 82.86%, cardiovascular drugs 66.67% of the prescribed drug which is similar to, 55.24% and 39.05% of drugs from blood forming organs and NSAIDS (Analgesics) respectively which was slightly higher than the study conducted by M Ashok Kumar et al. in tertiary teaching care hospital, Tamilnadu.[13] In our study, we found 42 Potential drug-drug interactions which is lower than the study carried out by M Ashok Kumar et al.[13]

CONCLUSION

The study have shown that majority of the patients with type 2 diabetes in Bharati Hospital were managed with Insulin monotherapy while the current OHA prescribing strategy do not achieve glycemic control on majority of the patient. Hence, combination therapies of Insulin with different OHAs were prescribed for proper glycemic control. The potential drug-drug interactions are frequent in type 2 diabetes mellitus and some of them deserve clinical attention. The actual and potential DDIs increase as per number of drugs in prescription. The management of clinically relevant DDIs can be improved by clinical pharmacist interventions. Advice on withdrawal or substituting the precipitant drug would be beneficial.

REFERENCES

1. Bertram G Katzung, Susan B. Masters and Anthony J Trevor. Basic and clinical pharmacology.2009; 11:727-50.

2. IDF diabetes atlas, http://www.diabetesatlas.org/content/sea-data.

3. Srishyla MV, Krishnamurthy M, Nagarani MA, Andrade C and Venkataraman BV. Indian J Pharmacol.1994; 26: 23-8.

4. R P Austin. Diabetes Spectrum. Jan 2006; 19(1): 13-16.

5. Ivan H Stockley. Stockley's drug interactions. 2002; 6:1-15.

6. Munichoodappa C. Epidemiology and burden of type 2 diabetes mellitus, Bangalore. Type 2 Diabetes theindian Scenario, Jayaram BM (Ed). Micro Labs 2002; P.13.

7. Vengurlekar S, Shukla P, Patidar P, Bafna R, Jain S. Prescribing pattern of antidiabetic drugs in Indore city hospital. Indian J Pharm Sci. 2008;70:637–40.

8. Willey CJ, Andrade SE, Cohen J, Fuller JC, Gurwitz JH. Polypharmacy with oralantidiabetic agents: An indicator of poor glycemic control. Am J Manag Care. 2006; 12:435–40.

9. Santhosh YL, Naveen MR. Medication Adherence Behavior in Chronic Diseases like Asthma and Diabetes Mellitus.International Journal of Pharmacy and Pharmaceutical Sciences. 2011; 3(3): 238-240.

10. Upadhyay DK, Palaian S, Ravi Shankar P, Mishra P, Sah AK. Prescribing pattern in diabetic outpatients in a tertiary care teaching hospital in Nepal. J Cardiovasc Dis Res. 2007; 4:248–55.

11. Arauz-Pacheco C, Parrott MA, Raskin P. Treatment of hypertension in adult patients with diabetes. Diabetes Care.2002; 25:134–47.

12. Lau GSN, Chan JCN, Chu PLM, Tse DCK, Critchley JAJH. Use of antidiabetic and antihypertensive drugs in hospital and outpatient settings in Hongkong.Ann- Pharmacother1996; 30:232-7.

13. M. Ashok Kumar*, A Nizar, K Shailaja, J Jayasutha, C Ramasamy. A study on prescribing   pattern and potential drug-drug interactions in type 2 diabetes mellitus (inpatients) in a tertiary care teaching hospital.DerPharmacia Lettre. 2011: 3 (4)13-19.

14. Adibe M.O. Aguwa C.N, UkweC.V, Okonta J.M, Udeogaranya P.O.Outpatient Utilization of anti-diabetic drugs in the south eastern Nigeria.Int.j.DrugDev& res. 2009. Sep-Dec; 1(1):27-36.

15. L. Sutharson, R.S. Hariharan, C. Vamsadhara. Drug Utilization Study in Diabetology Outpatient Setting of A Tertiary Hospital. Indian Journal of Pharmacology 2003; 35: 237-240.

16. Kannan, Arshad, SenthilKumarA Study on Drug Utilization of Oral Hypoglycemic Agents in Type-2 Diabetic Patients**.**Asian Journal of Pharmaceutical and Clinical Research. 2011; 4(4):61-65.

17. Hermann LS, Schersten B, Bitzen PO. Therapeutics comparison of metformin and sulphonylurea alone and in combinations. A double blind controlled study. Diabetes Care 1994; 17:1100-9.

18. RajeshwariS.AdhikariPrabha MR, pai M R S M, Drug utilization study in geriatric type 2 diabetic patients, journal of clinical and diagnostic research,2007 Oct ;1(5):440-443.