ORIGINAL ARTICLE

# Prospective, non-interventional, uncontrolled, open-chart, pharmacoepidemiologic study of prescribing patterns for anti-diabetic drugs at tertiary care hospital in Erode

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The aim of this study is to determine current prescribing patterns for anti-diabetic drugs adopted by physicians in Erode. The prospective, non interventional, uncontrolled, open-chart, pharmacoepidemiological study was conducted from January -2007 to April -2007 at a diabetic care centre having 350 diabetic patients. The pattern of prescribing anti-diabetic drugs was recorded along with glycosylated haemoglobin levels, total cholesterol, high-density lipoprotein, low-density lipoprotein, very low-density lipoprotein and triglycerides in insulin-dependent diabetes mellitus and non-insulin-dependent diabetes mellitus patients and the values were observed. The prescribing pattern of the oral anti-diabetic drugs shows that out of the various oral anti-diabetic drugs' available, drugs from only two groups were prescribed. Sulphonylureas, biguanides and combination therapy accounts for 31.43%, 20.28% and 33.71% of prescriptions, respectively, while insulin alone and with OAD's accounts for 6.28% and 8.29% prescriptions, respectively. Overall, prescribing trend is away from monotherapy with insulin and sulphonylureas and towards combination therapies.

**Key words:** Diabetes mellitus, oral anti-diabetic drugs, demographic profile, pharmacoepidemiologic

## INTRODUCTION

Diabetes mellitus is a complex heterogenous disorder or insulin dysfunction comprising various clinical subtypes and has multifactor aetiology. A variety of patho-physiological processes get affected in diabetes mellitus, resulting in alterations in several metabolic pathways. Globally, diabetes mellitus is assuming an epidemic proportion due to an increase in the population and general lifespan. The prevalence of the disease, especially of type 2 non-insulin-dependent diabetes mellitus (NIDDM), is very high.[1] It is associated with a myriad of complication and in most instances it need proper attention from an economical point of view as regarding diagnosis and treatment cost, than the actual disease itself. Drug therapy is the most commonly used method of any disease treatment in general practice. However, the patterns of drug prescribing are often inappropriate.[2,3] General practice database has been used as an effective method for pharmacoepidemiologic research.[4] Until 1990s, prescribers had two classes of drug to control hyperglycaemia (insulin and sulfonylurea). The introductions of other anti-diabetic drugs have further expanded the therapeutic arsenal.

Despite having used different methodologies that have estimated the future global trends in the frequency of diabetes mellitus generally agree that Asia is the major site of a rapidly emerging epidemic of diabetes.[5] India and China are, and will remain, the leading countries in terms of the number of people with diabetes mellitus in the year 2025. Among the 10 leading countries in this respect, 5 are in Asia. Although only a moderate increase in the total population in China is expected in the next 25 years, China is estimated to contribute almost 38 million people to the global burden of diabetes in the year 2025. India due to its immense population size and high diabetes prevalence will contribute 57 million. [6] The number of people with diabetes is increasing due to population growth, ageing, urbanization, increasing prevalence of obesity and physical inactivity. Surveys were generally performed in the middle-aged population and data were more limited at younger and older ages.

The introduction of new classes of medication to treat hyperglycaemia of type I and type II diabetes has found a place in the therapeutic armamentarium but details of their use patterns are not known. We sought to determine

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whether anti-hyperglycaemic prescribing patterns changed concurrently with new drug introduction and whether such changes were related to changes in the underlying patient population. The present study is based on the prescribing patterns related to their trends as of monotherapy or combination drug therapy, presumably in attempts to reduce the hyperglycaemic symptoms, directly impact the underlying disease pathogenesis and achieve better glucose control.

## RESEARCH DESIGN AND METHODS

A prospective, non-intervention uncontrolled open chart, pharmacoepidemiologic study included outpatients attending a diabetic care centre in Erode district of Tamil Nadu. A proforma to record the demographic profile of patients and the prescribing pattern of diabetic drug were prepared and standardized after a pilot study of 30 prescriptions which were independently analysed by various prescribes. The inclusion criteria were age, sex and prescribed diabetic drugs for the first time. The sugar level in blood and urine were estimated in the clinical pathology laboratory of the hospital. A total of 350 patients satisfying these criteria were enrolled during visits to the medical outpatient department during January 2007–April 2007.

The demographic profile of patients, documentation of their clinical history and the prescribing pattern of anti-diabetic drug were recorded on the standardized proforma by the undergraduate pharmacy student volunteers. Prescribers were unaware of the study and its objectives. Structured interviews with a questionnaire served as the main data collection method. In addition to receive an anti-diabetic drug, instructions regarding therapeutic life style changes and dietary therapy were given to men and women were noted. The numbers of patients prescribed for primary and secondary prevention of diseases were also studied. The patients were grouped according to the type of anti-diabetic drugs prescribed. All patients were included in four or five groups according to the prescribed anti-diabetic drugs. The documentary parameters included patient's age, sex, weight and height. Accordingly, baseline levels of fasting glucose, HbAIC, total cholesterol, HDL, LDL, VLDL and triglyceride were recorded. The patients were presented for follow-up on day 14, day 28, day 42, day 56, day 70, day 84 and day 98.

**Table 1: Laboratory results in NIDDM and IDDM patients**

| Type | IDDM | NIDDM |
|---|---|---|
| HbA1C (% of total Hb)* | 8.4 ± 2.4 | 8.8 ± 2.4 |
| Fasting glucose* | 172 ± 1.7 | 150 ± 1.7 |
| Total cholesterol (mg/dl)* | 184 ± 5 | 187 ± 5 |
| HDL (mg/dl)* | 52 ± 2 | 50 ± 2 |
| LDL (mg/dl)* | 26.2 ± 5 | 23.2 ± 5 |
| VLDL* | 32 ± 5 | 48 ± 5 |
| Triglycerides (mg/dl)* | 114 ± 7 | 103 ± 7 |

*Average of values found out every time on patient's visit

## RESULT

Of the 350 patients who received diabetic drugs, 58% were men (203/350) and 42% were women (147/350). The drug prescriptions, when classified according to patients age and sex, it was noted that there were more female patients in the age of 40-60 years (total 55.43% patients) when compared with males. The majority patients of the age >60 were male (total 29.14%). Nearly 50.57% patients had foot problems. The age of these subjects ranged from 31 to 96 years. Male were 103 and female were 74 in number. The risk for foot ulceration leading to amputation increased in people >40 who have had diabetes for 10 years or longer.[7] Sixty percent of patients with diabetes have some form of neuropathy, but in most case, (30–40%) there are no symptoms. The percentage of symptoms suggesting neuropathy was 30–40% in diabetes patients compared with 10% of people without diabetes.[8] At the baseline, the mean fasting blood sugar level (BSL) was 179.18 ± 73.25 and mean postprandial BSL 248.36 ± 62.21 for the severe cases. For the mild cases at the baseline, the mean fasting BSL was 132.25 ± 23.75 and mean postprandial BSL was 219.63 ± 48.32. Data given in Table 1 were the average of readings collected at every visit of patient on their follow-up to the hospital. HbA1C and VLDL were more frequency documented for insulin-dependent diabetes mellitus (IDDM), whereas triglyceride and forting glucose sere were found more often in NIDDM patients [Table 1, Figure 1].

It was found that of these 93.45% were receiving monotherapy and 6.45% were undergoing combination therapy [Table 2].

**Table 2: Details of diabetic drug prescribed**

| Type of diabetes | Type - I | | Type - 2 | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Drug prescribed | Group A insulin alone | | Group B insulin + OADs (sulfonylureas and thiazolidenidione) | | Group C sulfonylureas | | Group D biguanides | | Group E combination therapy | |
| Severity of disease | Severe | Mild | Severe | Mild | Severe | Mild | Severe | Mild | Severe | Mild |
| No. of patients | M – 10<br>F – 12 | M – 0<br>F – 0 | M – 16<br>F – 13 | M – 0<br>F – 0 | M – 0<br>F – 0 | M – 56<br>F – 64 | M – 0<br>F – 0 | M – 54<br>F – 26 | M – 43<br>F – 22 | M – 33<br>F – 20 |
| Percentage of prescription (%) | 6.28 | | 8.29 | | 31.43 | | 20.28 | | 33.71 | |

## DISCUSSION

Of the 350 patients who received diabetic drugs, 58% were men (203/350) and 42% were women (147/350). The prescription of drugs when classified according to their age and sex was noted that more female patients in the age of 40–60 years (total 55.43% patients) when compared with males. The majority patients of the age >60 were male (total 29.14%). It was seen that most of the females were affected due to the diabetes and were prescribed with the anti-diabetic drugs. Surveys were generally performed in middle-aged populations and older ages. Data on diabetes prevalence are usually presented in broad age bands, which suggest a biologically implausible step like increasing in diabetes prevalence with increasing age. Patients <60 years of age were nearly of 70.86% and patients >60 were 29.14%. Patients of nearly 28% were of IDDM (type 1) and 72% were of NIDDM (type 2).

Patients <60 years of age were nearly of 70.86% and patients >60 were 29.14%. Patients of nearly 28% were of IDDM (type 1) and 72% were of NIDDM (type 2). The age and body mass index were analysed. The medical reports sent out to the physicians are important document for basic data on the patients' stage in chronic conditions. Day *et al*.[9] reported that >40% of diabetic patients in general practice had no biochemical evaluation, eye or foot examination. In a randomized controlled trial, Hayes *et al*.[10] reported routine care in general. Practice for NIDDM patients is less satisfactory than care by hospital diabetic clinic, Single *et al.* Concentrating on the metabolic control of diabetic patients, Holland *et al*.[11] revealed that general practitioners providing care on an organized basis can reach a degree of glycaemic control equal to that reached by a hospital clinic. This implies that, in the absence the diagnosis in the medical report, the general practitioner cannot be sufficiently sure that the patient is free of these complications. Hyperglycaemia and glucose intolerance are the common links between various clinical subtypes and are due to various causes such as:

1. Overproduction of glucose because of enhanced glycogenolysis and gluconeogenesis. As both these pathways of glucose production are normally kept under inhibition by insulin, they get activated in insulin-deficient state.
2. Underutilization of glucose due to insulin deficiency or resistance.

Type 2 diabetes is associated with a loss of life of 5–10 years.[12] Diabetes is currently the fourth leading cause of death by disease in the United States. Type-II diabetes represents about 98% of all diabetes cases among persons older than 45 years of age,[13] approximately 18% in the range of 65 to 75 years of age and 40% of them older than 80 years of age.[14] Patients who are able to achieve good glycemic control with diet and exercise usually show significant improvement within six weeks and often have near-target blood glucose values within three months. However, this approach ultimately fails to control hyperglycemia in up to 90% of patients. When a patient does not show reasonable improvement within six weeks to three months of intervention with diet and exercise, pharmacotherapy should be added to the treatment plan.[15]

Biguanides and sulphonylureas have been traditionally used for the treatment of NIDDM or type 2 diabetes mellitus, but suffer from several pitfalls. In fact, biguanides are no longer recommended, as their use may result in a dangerous and often fatal complication, lactic acidosis.[16] Sulphonylureas are virtually the only drugs presently in use for the treatment of NIDDM, the most prevalent clinical subtype of diabetes mellitus, even though many patients do not show adequate response to the therapy initially (primary failure) or after some time (secondary failure). Moreover, their use may result in sustained and severe hypoglycaemia, cholestatic jaundice and various dermatological, haematological and allergic side effects.[17]

Therefore, search for more effective and safer hypoglycaemic agents has been felt, particularly after it was established that strict control of blood glucose levels slows the development and progression of the devastating chronic complications of diabetes mellitus. [18] With better understanding of the metabolic derangements of diabetes mellitus in recent year it became possible to develop more effective hypoglycemic agents, which act at various stages of the altered hormone-fuel homeostasis.

The regular therapy of insulin was given to the IDDM patients and the fasting glucose level, glycosylated hemoglobin levels, total cholesterol, HDL, LDL, VLDL and triglycerides were found out for IDDM and NIDDM

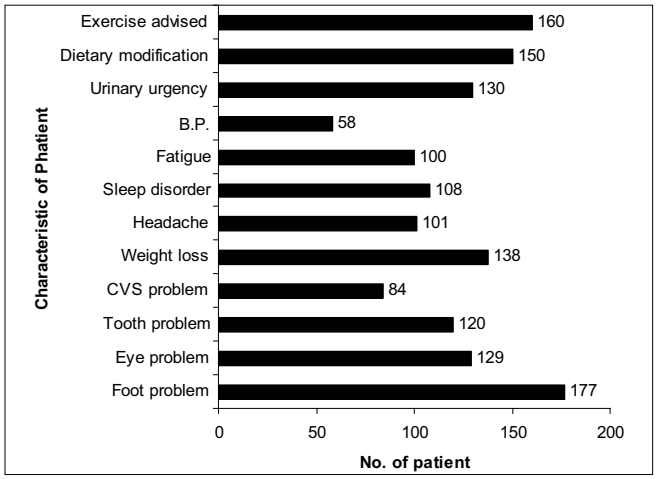


**Figure 1:** Statistical characteristics of patients

patients and the value was observed. The drugs prescribed for the IDDM and NIDDM patients were classified into five groups and the number of patients undergoing the monotherapy and combination therapy was noted. It was found that 93.45% were receiving monotherapy and 6.45% were undergoing combination therapy. The use of insulin monotherapy decreased (6.5%) than the use of insulin with any oral anti-diabetic drugs (OAD) (7.4%). Similarly, the prescription of sulphonylureas and biguanides was also decreased than the combination of sulphonylureas and biguanides.

In current practice, most physicians use HbA1C and fasting plasma glucose (FPG) when assessing glycaemic control. Recently, there is a great interest in including postprandial glucose in assessing overall glycaemic control for several reasons. In monotherapy, all pioglitazone, metformin and glipizide improve glycaemic control (HbA1C and FPG), but their effects on postload glycaemia are different. Prescription of sulfonylurea in monotherapy declined and its use in combination with biguanides and thiazolidinediones has been found to be increasing. This suggests that sulfonylurea monotherapy has been supplemented in part by combinations of sulphonylureas in newer drugs. Thus, there is evidence that clinicians are beginning to accept that combination therapies will be useful for achieving glycaemic targets.

It is well known that use of metformin and sulphonylureas in patients with renal insufficiency may be hazardous, increasing the risks of lactic acidosis and hypoglycaemia, respectively.[19,20] Therefore, the apparent of prescribing these drugs among patients with nephropathy would be expected. The prescribing pattern shows that of the various OADs available, drugs from only two groups were prescribed: sulphonylureas (31.43%) and biguanides (33.71%). The combination of these drugs accounts for 20.28% of the prescriptions. These findings were different than that of the western population where the drugs like rosiglitazone (thiazolidinedione) were also prescribed in considerable amount. Use of non-sulfonylurea insulin secretagogues (e.g., repaglinide, nitaglinide) and thiazolidinedione insulin sensitizers (e.g., troglitazone, rosiglitazone) has been reported in the countries like USA and UK.[21] In South India, among the thiazolidinediones, only selected drugs like pioglitazone were prescribed and that was also in very less amount. If we look at the drug utilization or prescribing trends of the OADs in the USA alone since 1990–2001; it shows that the sulfonylurea was the most prescribed drug (75.77%) till 1996. But after the entry of biguanides, especially metformin, in 1995 and thiazolidinedione insulin sensitizers in 1997, the proportion of description of sulfonylurea decreased, studied in 2001.

As per the survey held in Maharashtra (India), pioglar tablet was preferred in both males and females. Glimulin tablet was used more frequently in females. In our study, we have found that most preferred drug was metformin followed by glipizide. From Table 2 it is clear that the prescriptions with combination drugs are also increasing in number due to their advantages over monotherapy of OADs. Most prescribed combination is of metformin and glipizide.

Insulin therapy is prescribed for the IDDM patient. In our study, 6.28% prescription were of insulin alone, while 8.29% were of the insulin with OADs. These combinations were useful as the insulin monotherapy may cause the severe hypoglycaemia. Some of the prescription along with allopathic medication also contains diet restrictions for some patients. Studies on the dietary management were done in the other countries also, suggesting that the simultaneous use of the dietary management with the drugs will give better result in management of disease. [22]

Some patients were also advised the exercise for the sharp control over glucose level. It also helps in the control of weight as the use of some biguanides and thiazolidinediones may cause iatrogenic gain in weight.

## CONCLUSION

The anti-hyperglycaemic drug prescription pattern has changed in recent years and these changes are attributed to the introduction of different classes of medication in the market. Overall, the prescribing trend has been away from monotherapy with insulin and sulphonylureas and towards combination therapy, presumably in an attempt to reduce hypoglycaemic symptoms, directly impact the underlying disease pathogenesis and achieve better glucose control.

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