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CASE STUDY

Prescribing Trends Of Antidiabetics In Diabetic Patients And Hypertensive Diabetic Patients In An Urban Secondary Care Hospital

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ABSTRACT

Background: Diabetes is a chronic illness associated with significant morbidity and mortality. Diabetics are at a higher risk of polypharmacy and more vulnerable to irrational prescribing especially diabetics suffering from concurrent illnesses like hypertension. **Objectives**: The present study was conducted with the objectives of providing an insight into the current use of antidiabetic medications to diabetics and hypertensive diabetics in urban areas and determining how the patient factors influence the prescribing of antidiabetic medications. **Methods**: A retrospective epidemiological study was arried out at Out-Patient Department (OPD) at Shri Vraj Hospital, Baroda, Gujarat, India, from January 2008 to March 2008. Data of patients of past two years were collected. The details were entered in the structured patient profile form. Data were statistically analyzed using the SPSS software. **Results**: Data of 492 patients were collected and analyzed of which 334 (67.88 %) were males and 158 (32.11 %) were females. These patients were further categorized based on their age. 126 patients (25.6 %) belonged to the age group 20 - 44 years, 294 (59.75 %) to the age group 45 - 65 years and 72 (14.6 %) to the age group 65 – 80 years. 246 (50%) patients out of the 492 patients studied were suffering from coexisting hypertension. Co-existing hypertension was found to be more prevalent in the age group 45 - 65 years (59.75%) and its incidence was found to be more in females (56.32%). Metformin was the oral hypoglycemic which was the highest prescribed. Metformin and Acarbose were prescribed to obese patient. Sulphonylureas and thiazolidnediones were prescribed less in obese patient. In elderly patients sulphonylureas were prescribed less. In hypertensive diabetics Metformin and Pioglitazone were most frequently prescribed drugs. Monotherapy was prescribed for 11.3% patients and remaining patients were prescribed combination therapy. **Conclusion**: Biguanides and Insulin were the most commonly prescribed antidiabetics. A combination of two or more drugs of different classes was prescribed to hypertensive diabetics. Since the scope of the present study is limited as the number of patients studied is less, extensive studies are required to confirm our findings.

Keywords: Diabetes Mellitus, Metformin, Body Mass Index (BMI), hypertensive diabetics, oral hypoglycemics.

INTRODUCTION

Diabetes is increasing in prevalence and currently affects more than 170 million people worldwide[1]. About 90% of sufferers have type 2 diabetes[2]. Both type 1 and type 2 diabetes are chronic conditions and have devastating complications mostly due to accelerated macrovascular and microvascular diseases[3].

India is expected to garner the dubious distinction of having the highest number of diabetics in the world by 2025. India's 32 m diabetics account for one-fourth of the global diabetic population. These numbers are estimated to grow to 57.2 m by the year 2025[4].

In India, treatment of Diabetes is often started by a general practitioner (GP). Changing lifestyle and dietary measures are usually the first step. The second step is 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 α-glucosidase-inhibitors. After 1999, two new groups of drugs, i.e. Meglitinides (Repaglinide,

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Nateglinide) and Thiazolidinediones (Rosiglitazone, Pioglitazone) became available[5]. 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. Also many patient factors like age, sex, BMI and coexisting illnesses determine the prescription[6].

Also there are many international and national guidelines which provide evidence-based recommendations for the treatment of diabetes[7].

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 [8]. Hence it becomes essential to ascertain a proper management of diabetes. A study of factors 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. 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[9]. Hypertension (HT) is frequently associated with diabetes mellitus (DM) and its prevalence doubles in diabetics compared to the general population. This high prevalence is associated with increased stiffness of large arteries, which often precedes macrovascular events[10]. The rapidly growing number of patients with coexisting diabetes and hypertension must be intensively treated to protect them from their very high risk for premature cardiovascular morbidity and mortality[11].

Thus this study was undertaken to find out the trends of prescribing antidiabetics in urban areas in India and what factors determine the prescribing of a particular antidiabetic drug or a combination of multiple drugs.

MATERIALS AND METHODS

A retrospective observational epidemiological study was undertaken for three months (January – March 2008) in outpatient department of Shri Vraj hospital, Baroda. Prescriptions of diabetic patients being treated at the hospital during past two years were included in this study.

Patient inclusion criteria:

- Patients suffering from Type 1 and Type 2 Diabetes mellitus attending OPD in Shri Vraj Hospital.
- Diabetic patients of both sexes.
- Diabetic patients of all ages between 18 years and 65 years.
- Diabetic patients having concurrent illnesses like hypertension.

Patient exclusion criteria:

- Pregnant females suffering from Diabetes.
- Diabetic patients suffering from complications of diabetes like retinopathy, neuropathy and diabetic foot.

After collecting the data, the details were entered in the structured patient profile form. The patients were classified into different age groups of 25-44 years. 45-65 years and age above 65 years

The data was classified as:

1- The different oral hypoglycemic drugs prescribed to diabetic patients depending on various factors such as age, sex and Body Mass Index (BMI).

2- The different oral hypoglycemic drugs prescribed to hypertensive diabetics based on factors such as age and sex.

Statistical Analysis: SPSS ver. 14 (Statistical package for Social Sciences Inc., USA) software package was used for data stratification and analysis and Chi square test was applied on data where the *p* value less than 0.05 was considered significant.

RESULTS

1. **Characteristics of study population**:

Data of 492 patients were collected and analyzed of which 334 (67.88 %) were males and 158 (32.11 %) were females. These patients were further categorized based on their age. 126 patients (25.6 %) belonged to the age group 20 - 44 years, 294 (59.75 %) to the age group 45 - 65 years and 72 (14.6 %) to the age group 65 – 80 years. 246 (50%) patients out of the 492 patients studied were suffering from coexisting hypertension. Co-existing hypertension was found to be more prevalent in the age group 45 - 65 years (59.75%) and was found more in females (56.32%)

2**. Distribution of patients based on BMI**

It was observed that 16.70% patients were having their BMI in range 30-35 and 3.71% in the range of 35-40. Thus 20.41% patients were obese. (**Table 1**)

Table 1: Distribution of patients based on BMI

BMI (kg/ m2)	Number of patients	%
< 20	31	6.39 %
20 – 25	154	31.75 %
25 – 30	201	41.44 %
30 – 35	81	16.70 %
35 – 40	18	3.71 %
Total	485	100 %

3. **Percentage frequency distribution of anti-diabetic medicines with relation to age group of patients**

We observed that Metformin was the highest prescribed antidiabetic in patients of all the age groups. Also it was observed that Insulin was prescribed more in the age group 20-44 years and as the age advanced the number of patients prescribed Insulin decreased. This result is statistically significant and indicates that age is an important factor influencing the prescription of insulin. Similarly statistically significant evidence is also available to show that age influences the prescription of oral hypoglycemic drugs like Glibenclamide, Glipizide, Rosiglitazone and Acarbose. (**Table 2**).

Table 2: Percentage frequency distribution of anti-diabetic medicines based on age group of patients

Medicines	20-44 years		45-65 years		> 65 years		Total		Chi-square result
	number	%	number	%	number	%	number	%	P-value
Insulin Injection	86	68.30%	72	24.50%	14	19.40%	172	35.00%	0*
Glibenclamide	3	2.40%	13	4.40%	7	9.70%	23	4.70%	0.0599
Gliclazide	34	27%	99	33.70%	22	30.60%	155	31.50%	0.39374
Metformin	101	80.20%	224	76.20%	49	68.10%	76	76.00%	0.15774
Glimepiride	24	19%	80	27.20%	17	23.60%	121	24.60%	0.20057
Glipizide	11	8.70%	37	12.60%	18	25.00%	66	13.40%	0.00435*
Pioglitazone	25	19.80%	85	28.90%	16	22.20%	126	26.60%	0.11551
Rosiglitazone	8	6.30%	28	9.50%	14	19.40%	50	10.20%	0.01149*
Acarbose	24	19%	52	17.70%	3	4.20%	79	16.10%	0.03*
Number of patients	126		294		72		492		

*[* Statistically significant results; P value < 0.05]*

4. **Percentage frequency distribution of anti-diabetic medicines with relation to sex of patients**.

It is evident from the table 3 that Metformin was the highest prescribed antidiabetic drug and Glibenclamide was the least prescribed antidiabetic to patients of both the sexes. The prescription of Glipizide was influenced by the sex of the patient as the statistically significant evidence suggests. (**Table 3**)

Table 3: Percentage frequency distribution of anti-diabetic medicines based on sex of patients.

Medicines	Males		Females		Total		Chi-square result
	number	%	number	%	number	%	P-value
Insulin Injection	125	37.40%	47	29.70%	172	35.00%	0.04538*
Glibenclamide	16	4.80%	7	4.40%	23	4.70%	0.85446
Gliclazide	103	30.80%	52	32.90%	155	31.50%	0.64395
Metformin	247	74.00%	127	80.40%	374	76.00%	0.01189*
Glimepiride	87	26%	34	21.50%	121	24.60%	0.27608
Glipizide	37	11.10%	29	18.40%	66	13.40%	0.02702*
Pioglitazone	82	24.60%	44	27.80%	126	25.60%	0.43401
Rosiglitazone	35	10.50%	15	9.50%	50	10.20%	0.73556
Acarbose	54	16.20%	25	15.80%	79	16.10%	0.9225
Number of patients	334		158		492		

[Statistically significant results; P value < 0.05]

5. **Percentage frequency distribution of anti-diabetic medicines with relation to BMI group of patients (BMI in kg/m^2)**

It can be inferred from statistically significant evidence that BMI influences the prescription of Metformin, Gliclazide and Pioglitazone. (**Table 4**)

Table 4: Percentage frequency distribution of anti-diabetic medicines based on BMI group of patients (BMI in kg/m$^{2)}$

Antidiabetic drugs	< 20		20 - 25		25 - 35		30 – 35		35 - 40		Total		Chi-square result
	Number	%	Number	%	Number	%	Number	%	number	%	Number	%	P-value
Insulin	18	58.10%	61	39.60%	56	27.90%	31	38.30%	2	11.10%	168	44	0.00116*
Glibenclamide	2	11.10%	5	8.20%	2	3.60%	2	6.70%	0	0%	11	6.	0.76797
Gliclazide	1	5.60%	14	23%	10	17.90%	4	12.90%	2	100%	31	18	0.01528*
Metformin	11	61.10%	35	57.40%	34	60.70%	28	90.30%	0	0%	108	64	0.00609*
Glimepiride	0	0%	4	6.60%	9	16.10%	4	12.90%	0	0%	17	10	0.23552
Glipizide	0	0%	4	6.60%	3	5.40%	1	3.20%	0	0%	8	4	0.80183
Pioglitazone	0	0%	10	16.40%	2	3.60%	7	22.60%	0	0%	19	11	0.0225*
Rosiglitazone	1	6%	3	4.90%	2	3.60%	6	19.40%	0	0%	12	7	0.06836
Acarbose	0	0%	9	14.80%	4	7.10%	6	19.40%	0	0%	19	11	0.18182

[Statistically significant results; P value < 0.05]

6**. Percentage frequency distribution of various oral hypoglycaemics given with relation to age group of patients suffering from diabetes and hypertension.**

It was found that age of patient influences the prescription of Glimepiride and Glipizide and that the prescription of Glimepiride, Pioglitazone and Acarbose decreases as age increases in hypertensive diabetics. It is evident that Metformin was the highest prescribed drug in total population of hypertensive diabetics and also in all the age groups and the age of the patient does not influence its prescription. Also it can be observed that Glibenclamide was the least prescribed drug in total population of hypertensive diabetics. (**Table 5**)

Table 5: Percentage frequency distribution of various oral hypoglycaemics given based on age group of patients suffering from diabetes and hypertension

Medicines	20-44 years		45-65 years		> 65 years		Total		Chi-square result
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	P-value
Glibenclamide	0	0%	5	3.90%	4	10.50%	4	5.00%	0.18272
Gliclazide	5	41.70%	33	25.60%	13	34.20%	51	28.50%	0.33813
Metformin	12	100%	108	83.70%	32	84.20%	152	84.90%	0.31819
Glimepiride	8	66.70%	53	41.10%	7	18.40%	68	38.00%	0.00432*
Glipizide	4	33.30%	14	10.90%	12	31.60%	30	16.80%	0.00307*
Pioglitazone	4	33.30%	37	28.70%	9	23.70%	50	27.90%	0.75935
Rosiglitazone	1	8.30%	18	14.00%	5	13.20%	24	13.40%	0.86016
Acarbose	4	33.30%	30	23.30%	3	7.90%	37	20.70%	0.06452
No of Patients	27		176		43		241		

[Statistically significant results; P value < 0.05]

7. **Percentage frequency distribution of oral hypoglycaemics given with relation to sex of patients suffering from diabetes and hypertension**.

Statistically significant evidence shows that sex of the patient influenced the prescription of Gliclazide. (**Table 6**)

Table 6: Percentage frequency distribution of oral hypoglycaemics given based on sex of patients suffering from diabetes and hypertension.

Medicines	male		Female		Total		Chi-square result
	number	percent	number	Percent	number	percent	P value
Glibenclamide	7	6%	2	3.20%	9	5.00%	0.40302
Gliclazide	27	23.30%	24	38.10%	51	28.50%	0.03592*
Metformin	97	83.60%	55	87.30%	152	84.90%	0.51107
Glimepiride	50	43.10%	18	28.60%	68	38.00%	0.05574
Glipizide	16	77.80%	14	83.20%	30	12.19%	0.14931
Pioglitazone	30	25.90%	20	31.70%	50	27.90%	0.40206
Rosiglitazone	16	13.80%	8	12.70%	24	13.40%	0.83735
Acarbose	21	18.10%	16	25.40%	37	20.70%	0.2498

Number of patients	157	89	246

[Statistically significant results; P value < 0.05]

8**. Combinations of antidiabetics prescribed.**
Out of the various combinations of antidiabetic drugs which were prescribed the following combinations were the most frequently prescribed: Insulin + metformin (12.8% patients), metformin + glimepiride (8.7%), metformin + gliclazide + pioglitazone (7.9%), insulin + gliclazide (5.9%) and gliclazide + metformin (5.5%).

DISCUSSION

Demographic data of patients reveal that co existing hypertension was found to be more prevalent in the age group 45 - 65 years (59.75%) and was found more in females (56.32%). From the distribution of patients based on their Body mass index (BMI) it was observed that 20.41% patients suffering from diabetes were obese (BMI value greater than 30). Our results matched with a study published in The Journal of American Medical association (JAMA) [12]. Their results showed in 2001 that the prevalence of obesity (BMI greater than 30) in diabetic patients was 20.9% as against 19.8% in 2000, an increase of 5.6%. Overweight and obesity were significantly associated with diabetes. In our study the patients with BMI greater than 30 were 20.41% and prevalence of BMI of 40 was 1.8%[13].

One important result stemming from our study was that age was found to be an important factor influencing the prescription of drugs like Metformin, Insulin, Glipizide, Rosiglitazone and Acarbose. It was evident that the frequency of prescription of insulin and Acarbose was more in the younger patients and these drugs were prescribed less as the age increased. Our results correlate with the results of a study carried out by Jean-Louis Chiasson- "The Efficacy of Acarbose in the Treatment of Patients with Non-Insulin-dependent Diabetes Mellitus: A Multicenter Controlled Clinical Trial" wherein it was found that acarbose improved long-term glycemic control in patients with non-insulin-dependent diabetes mellitus regardless of concomitant antidiabetic medication [13]. Thus we can justify the high frequency of prescription to younger patients as a measure of preventing long term complications and for facilitating a better glycemic control in a combination therapy. For Rosiglitazone, Glipizide and Gliclazide the frequency of their prescription was highest in patients with age greater than 65 the reason for this trend is that the long-acting sulphonylureas like Chlorpropamide and Glibenclamide are associated with a greater risk of hypoglycaemia, for this reason they should be avoided in the elderly and shorter-acting alternatives, such as Gliclazide or Glipizide or drugs from other class should be used[14].

Metformin was most prescribed to patients in the age group 45-65 years. The reason for this can be attributed to the fact that with increased age the risk of hypoglycemia and its incidences increases in patients treated with sulphonylureas monotherapy and even in combination therapy of sulphonylurea and any other oral hypoglycemic drug. Thus Metformin is preferred over Sulphonylureas in this age group[15].

Another interesting observation was that Metformin was prescribed more to females than to males. It was prescribed to 74% of total males and 80.40% of total females. One reason for such a trend is the intriguing finding of a study carried out in the Netherlands that female patients discontinued sulphonylureas more frequently to avoid weight gain mainly as a result of edema and reduction of the osmotic diuresis caused by hyperglycemia. The discontinuation rate in females of 25% is much larger than expected from tolerability data of clinical trials, which showed that 10–15% of patients discontinued sulphonylureas because of adverse effects[5]. Therefore to avoid non-compliance of sulphonylureas by females Metformin was prescribed more frequently to females to ensure a uniform glycemic control.

When the influence of BMI (body mass index) on drug prescription was reviewed, results show that only Metformin and Acarbose were prescribed to patients whose BMI values were between 30 and 40 and sulphonylureas and Pioglitazone were not prescribed. It is a well accepted fact that sulphonlyureas and Thiazolidinediones cause excess weight gain and thus are not preferred in obese patients[16].

It was found that Metformin was prescribed to 90.30% of the total patients whose

BMI was greater than 30 (obese). As the BMI increased the frequency and number of prescriptions also increased. The reason which can be attributed to this finding is that Metformin does not cause weight gain but sulphonylureas and Thiazolidinediones cause excess weight gain and hence they are not preferred for obese patients. In September 1998, the United Kingdom Prospective Diabetes Study (UKPDS) research group published the results of intensified treatment of diabetes and demonstrated the beneficial effects of Metformin in overweight Type 2 diabetes patients[17]. Thus our results correlate with the UKPDS research group findings. Worldwide, the UKPDS results changed the existing ideas of treating Type 2 Diabetes Mellitus. In 1999, the NHG guideline was thoroughly revised in line with the results of the UKPDS study. In the revised guideline, a distinction in pharmacological treatment was made for patients with a BMI above and below 27 kg m^{-2}. Lean patients (BMI < 27 kg m^{-2}) were advised to start initial treatment with a sulphonylurea, such as Tolbutamide or Gliclazide. For obese patients (BMI ≥ 27 kg m^{-2}) the recommendation was to start with Metformin. When monotherapy failed, a combination of Metformin and sulphonylurea was considered appropriate[18]. Hypertension (HT) is frequently associated with diabetes mellitus (DM) and its prevalence doubles in diabetics compared to the general population. The number of patients suffering from coexisting hypertension was 246 (50%) of the total population of 492. A tight blood glucose control is advised because coexisting hypertension increases the risk of development of complications and hypoglycemia. Hence Metformin is normally given along with insulin. It was found that Metformin was prescribed more to hypertensive females (87.30 %) than to hypertensive males (83.60%). Glimepiride was prescribed more to males (43.10%) and less to females (28.6%) similarly in case of Glibenclamide more males (6%) were prescribed the drug than females (3.20%). The reason for this can be attributed to the fact that a greater incidence of non-compliance is observed among hypertensive diabetic females for sulphonlureas due to the excess weight gain induced by those drugs, thus to ensure compliance and tight glycemic control Metformin was prescribed to hypertensive females and sulphonylureas to hypertensive males[5]. Out of the various combinations of antidiabetic drugs which were prescribed the following combinations were the most frequently prescribed: Insulin + Metformin (12.8% patients), Metformin + Glimepiride (8.7%), Metformin + Gliclazide + Pioglitazone (7.9%), Insulin + Gliclazide (5.9%) and Gliclazide + Metformin (5.5%). A similar study as ours conducted by KA Al Khaja, RP Sequeira, and VS Mathur concluded that as combinations, sulfonylureas plus Metformin was most popular, followed by Metformin plus Insulin, and sulfonylureas plus Insulin [19].

IMPLICATIONS OF THIS STUDY

This study has provided a baseline data regarding the prescribing pattern in diabetic and hypertensive diabetic patients in an urban secondary care hospital. Since diabetes and co-existing hypertension in diabetes is widespread problem in India, this study has provided a scope for further research in this area.

LIMITATIONS

This study has few limitations. The diabetic in-patients were not included in this study and the follow up prescriptions were not included in this study. Hence similar studies covering large number of patients are needed to confirm our findings.

CONCLUSION

The prescribing pattern shows that combination of antidiabetics are prescribed more to achieve a better glycemic control in order to avoid long term complications.

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