



PHARMACOEPIDEMIOLOGICAL ASSESSMENT OF INSULIN THERAPY IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

Insulin administration was found to be better choice for diabetic patients who started surviving for longer periods with diabetes. The study aims to assess the prescribing pattern of insulin therapy among Type 2 Diabetes Mellitus Patients. A retrospective case analysis was conducted in medical record department of tertiary care teaching hospital. A total of 190 case records of diabetic patients with insulin therapy were reviewed and evaluated using descriptive statistics, mean and standard deviation. Out of 190 study population, male patients were more (52.63%). More number of prescriptions prescribed for the age group of 40-60 years (48.96%) with a mean \pm SD of age 54.11 ± 12.26 . Most of them were diabetic (60.53%) followed by pre-diabetic (22.63%) with a mean \pm SD of GRBS range 246.61 ± 109.72 . More number of prescriptions were with only insulin (56.32%) than in combination with OHA (43.68%). The most common insulin preparation was found to be insulin human actrapid (70.53%). Most of the prescription containing insulin actrapid and insulin mixtard (82.35%) followed by Insulin actrapid and insulin NPH (11.76%). The most commonly prescribed OHA was biguanides (47.17%). The most commonly prescribed combination of OHA was Biguanides + Sulphonylureas. We found that drug utilization pattern of insulin was optimal and effective, which helps to reduce high blood sugar level and to prevent further complications.

KEYWORDS: Diabetes Mellitus, Insulin, OHA, Pharmacoepidemiology.

INTRODUCTION

Diabetes mellitus is a pandemic disease that has struck each and every corner of the world. According to the ICMR Indian Diabetes study, a national diabetes study, India currently has 62.4 million people with diabetes. Various classes of antidiabetic drugs including insulin and OHA are currently used in the treatment of diabetes, which acts by different mechanisms to reduce bloodglucose levels to maintain optimal glycaemic control.^[1]

Although insulin may be the first agent prescribed to patients with type 2 diabetes who have marked hyperglycemia, oral antidiabetes drugs are usually the first pharmacologic treatment. In general, these drugs are first prescribed as monotherapy, however, combination therapy with two oral antidiabetes drugs with different mechanisms may also be a first-line option. Unfortunately, oral antidiabetes drugs have limited efficacy for long-term glucose lowering and, therefore, many patients may require insulin to achieve better metabolic control. There are several factors that may account for the need to initiate insulin therapy in patients taking oral antidiabetes drugs, including progressive β -cell failure, deterioration of insulin sensitivity because of

glucose toxicity or the development of resistance to the oral antidiabetes drug.^[2]

Different type of insulin preparations such as neutral insulin, biphasic insulin, isophane insulin etc. and antidiabetic drugs such as sulphonylureas, biguanides, and thiazolidinediones are the commonly used medication for the treatment of DM. Insulin therapy is mainly used for treating the patients with type 1 diabetes and type 2 diabetic patients. Oral hypoglycemic agents used for the treatment of type 2 DM are divided in to seven different class like Sulphonylureas, Short-acting insulin Secretagogues, Biguanides, alpha-Glucosidase inhibitors, and Thiazolidinediones etc are belonging to the older class of oral hypoglycaemic agents and dipeptidyl-peptidase-4 inhibitor (DPP-4), Exenatide are belonging to the newer class. But some patients with type 2 DM not respond to the oral hypoglycemic agents and some patients shows the decreasing response during therapy. These patients require the treatment with the insulin.^[3]

However, delay in insulin initiation is common. About 50% of patients with poor control T2DM did not timely start insulin therapy and the initiation was usually three

to five years after failure of oral hypoglycemic agents. There are many factors influencing delayed insulin initiation including those caused by healthcare providers and its system, as well as the patients themselves.^[4]

Several studies have been carried out regarding the prescription pattern of antidiabetic drugs in South India. But only a few studies were carried out regarding the drug utilization pattern of insulin therapy among type 2 diabetes mellitus patients.

In this context we decided to conduct the study to assess the prescribing pattern of insulin by retrospectively analyzing the management of antidiabetic therapy in a patient cohort and thereby improving health related quality of life of diabetes mellitus patients.

MATERIAL AND METHODS

The study was carried out for a period of six months. A retrospective case analysis was carried out by reviewing prescriptions of 190 patients who have been prescribed with insulin for treating Type 2 Diabetes Mellitus. The study was approved by Institutional Ethics Committee of Navodaya Medical College Hospital & Research Centre, Raichur

Inclusion Criteria

- Case records of patients prescribed with insulin from 2014 January to 2016 December.

Exclusion Criteria

- Case reports of Out-patients.
- Pregnant and lactating women.
- Paediatric patients.

Retrospective data from patient's case files were obtained with regard to GRBS range, type of antidiabetic treatment, insulin preparations, types and combination of oral hypoglycemic agents etc.

The demographic data, disease data and drug data of the patients were analyzed. Data was analysed using descriptive statistics i.e, total numbers, percentage, mean and standard deviation to represent prescribing pattern.

RESULTS AND DISCUSSION

A total number of 190 case sheets of diabetes mellitus patients prescribed with insulin therapy were reviewed and analyzed.

Out of 190 patients 100 (52.63%) were male and 90 (47.37%) were female prescribed with insulin. This data suggests that male patients are more suffered by diabetes mellitus than that of females. One of the major reasons for this was obesity and fat deposition, which is strongly linked to insulin resistance. Both of these factors are tend to observe more in males compared to females. The result stated was similar to the study conducted by **Harikrishnan KV et al.** and **Himaja et al.**

The maximum number of patients was found in the age group of 40-60 years (48.96%), 60-80 years (41.05%), 20-40 years (7.89%) and least were found in the age group of 0-20 years (1.05%) and greater than 80 years (1.05%). The mean age of the patients were 54.11 (± 12.26). This data suggests that middle aged and older adults are at higher risk due to combined effects of increasing insulin resistance and impaired pancreatic islet function with aging associated with age related adiposity and physical inactivity. These findings were similar to the study conducted by **Thomas NJ et al.** and **Himaja et al.**

Majority of patients were admitted in the hospital due to fever 46(25.56%), giddiness 31(17.22%), polyuria 24(13.33), weakness 17(9.44), foot ulcer 17(9.44), tingling and numbness 17 (9.44), eye problems 16(8.89), polyphagia 7 (3.89) and polydipsia 5 (2.79) respectively. These findings suggest that most of the patients came with symptoms of diabetes such as polyuria, weakness, non healing foot ulcer, tingling and numbness, eye problems, polyphagia and polydipsia.

Figure 1 shows the known history 139 (73.16%) and non history 51(26.84) of type 2 diabetes mellitus. Most of the known history patients were already on treatment.

190 subjects were categorized into normal 32(16.84%), pre-daibetic 43(22.63%) and diabetic 115(60.53%) based on GRBS range, which was stated in **table 1**. The mean GRBS range of patients was 246.61(± 109.72). This data suggests that the prevalence of diabetes patients (uncontrolled type 2 diabetes mellitus) was more in the study followed by pre-daibetic patients. This result was supported by the study done by **Jahagridar SS et al.**

Figure 2 illustrates patients prescribed with insulin alone 107 (56.32%) and insulin in combination with other oral hypoglycemics 83(43.68%). This data shows that most of the patients were on insulin monotherapy rather than insulin and OHA (combination therapy) due to the fact that majority of the sudy population has uncontrolled type 2 diabetes mellitus. Since the current study was done in the inpatients prescription thereby providing the advantage of close monitoring while the patients were been hospitalized. Similar result was found in the study conducted by **Thomas NJ et al.**

Majority of the patients prescribed with insulin human actrapid 146 (70.53%), insulin human mixtard 57 (27.53%), Insulin glargine 2(0.97%) and NPH insulin 2 (0.97) as shown in **figure 3**. This data can be understood by the fact that the treatment with fast acting insulin preparation due to the fact that it doesn't remain in the body as long as regular insulin does and also results in fewer episodes of hypoglycemia. This result in our study was strongly supported by the study conducted by **Agarwal AA et al.**

Among different types of oral hypoglycemic agents, most of the patients were prescribed with biguanides 75(47.17%) followed by sulfonylureas 56(35.22%), Alpha-glucosidase inhibitors 20 (12.58%), Dipeptidyl peptidase 4 inhibitors 5(3.14%), Meglitinides 2(1.26%) and Thiazolidinediones 1 (0.63%). This data suggests that majority of patients prescribed with biguanides and sulfonylureas which may be due to its advantages like no weight gain, no hypoglycemia etc. and its low cost when compared to other OHA. The similar result was stated in the study conducted by **Agarwal AA et al.** and **Thomas NJ et al.**

Most of the prescription containing insulin actrapid and insulin mixtard 14(82.35%) followed by Insulin actrapid and insulin NPH 2(11.76%) and Insulin mixtard and insulin glargine 1(5.89%) as stated in **table 2**. This combination of insulin was observed in inpatient prescriptions mainly due to the fact that it ensures close monitoring and posing a greater degree of safety to the patients as they are hospitalized. This study result was similar to the study conducted by **Thomas NJ et al.**

Table 3 shows the distribution of combination of oral hypoglycemic agents. In which Biguanides+

Sulfonylureas was prescribed more 38(69.09%) followed by sulfonylureas + Biguanides+Alpha glucosidase inhibitors 10(18.18%), Biguanides+Alpha glucosidase inhibitors 5(9.09%), Biguanide+ Dipeptidyl peptidase 4 inhibitors 1(1.82), Biguanides + Sulphonylureas + Thiazolidnedions 1(1.82). This data suggests that patients are mostly prescribed with biguanides + sulfonylureas (dual combination therapy) than other dual and triple combination therapy which may be due to its fewer side effects and also due to lesser cost. This finding was similar to the study conducted by **Thomas NJ et al., Agarwal AA et al.** and **Guidoni CM et al.**

In macrovascular complications, patients with hypertension was more 75(72.12%) followed by cardiovascular diseases 19(18.27%) and cerebrovascular diseases 10(9.61%) as illustrated in **table 3**. The microvascular complication of diabetes, where renal disorders was found to be more 11(64.70%) followed by eye disorders 3 (17.65%) and neurological disorders 3 (17.65%) as shown in **table 4**. This data suggests that more than half of the patients were suffering with diabetic complications in different system which may be due to their long standing and uncontrolled diabetes mellitus.

FIGURES

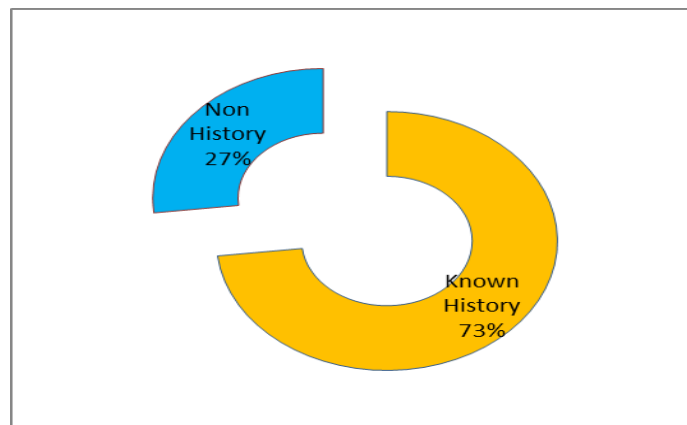


Figure 1: History of Type 2 Diabetes mellitus (n=190).

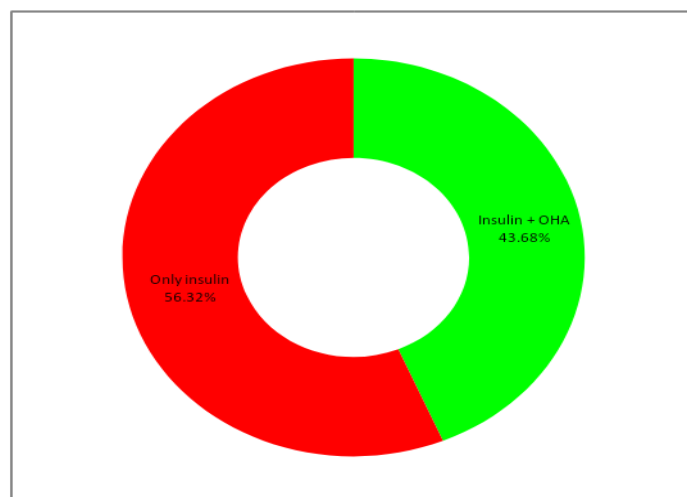


Figure 2: Combination of Insulin and OHA (n=190).

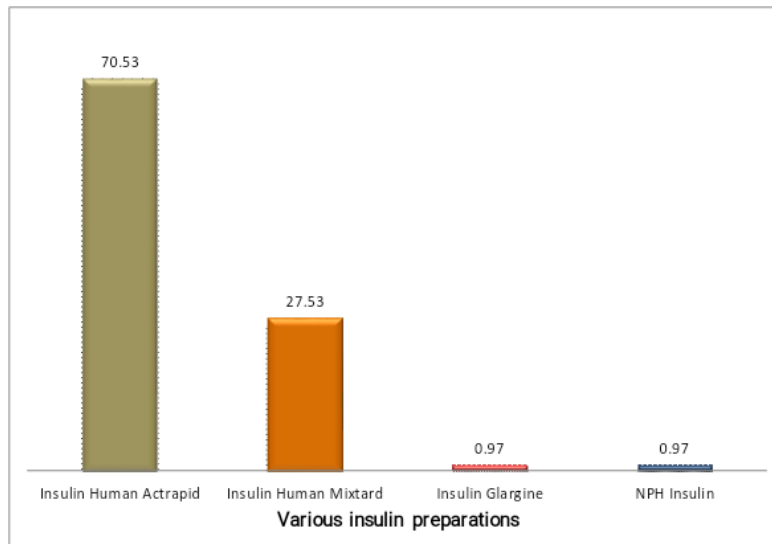


Figure 3: Various Insulin Preparations (n=207).

TABLES

Table 1: Categorization based on GRBS range (n= 190).

Sl.No	Category	No: of cases	Percentage (%)
1	Normal (70-160)	32	16.84
2	Pre- Diabetic (160-200)	43	22.63
3	Diabetic (> or = 200)	115	60.53
		Mean = 246.61 SD = 109.72	

Table 2: Commonly prescribed insulin combinations (n=17).

Sl.No	Insulin preparations	No: of prescriptions	Percentage(%)
1	Insulin Actrapid+ Insulin Mixtard	14	82.35
2	Insulin Actrapid + Insulin NPH	2	11.76
3	Insulin mixtard+Insulin glargine	1	5.89

Table 3: Macrovascular Complications of Diabetes (n=104).

Sl.No	Complications	No: of patients	Percentage (%)
1	Cerebrovascular diseases	10	9.61
2	Cardiovascular diseases	19	18.27
3	Hypertension	75	72.12

Table 4: Microvascular Complications of Diabetes (n=17).

Sl.No	Complications	No: of patients	Percentage (%)
1	Eye disorder	3	17.65
2	Renal disorder	11	64.70
3	Neurological disorders	3	17.65

CONCLUSION

We found that diabetic patients were treated with both monotherapy and combination therapy. In monotherapy, insulin was most commonly prescribed drug followed by Biguanides and Sulphonylureas. Drug therapy should be aimed at treating both the complication and existing condition rather either alone. The drug prescribing pattern for Type 2 Diabetes Mellitus patients were found to be effective to reduce their high blood sugar level and to prevent complications.

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