SUSPECTED ADR MONITORING AND COMPARATIVE ASSESSMENT OF ANTIDIABETIC DRUGS ON GLYCEMIC CONTROL IN TYPE 2 DIABETIC PATIENTS

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INTRODUCTION

DIABETES MELLITUS

Diabetes mellitus (DM) commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period. Diabetes mellitus is the most common endocrine disorders affecting million people worldwide. It is a chronic condition, characterized by hyper-glycemia, due to impaired insulin secretion. It is a disease that affects the body ability to produce or use of insulin. Insulin is a hormone. When the body turns the food you eat into energy (sugar or glucose), insulin is released to help transport this energy to the cells. Its chemical message tells the cell to open and receive glucose. If the insulin produce is little or no production, leads too much sugar remains in your blood (hyper glycaemia). Blood glucose levels are higher than normal for individuals with diabetes. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart and blood vessels. [1]

There are two types of diabetes: -

Type 1(also know as insulin dependent diabetes mellitus) Type 2(also known as non-insulin dependent diabetes mellitus)

Type 1 diabetes: - This type of diabetes mellitus is also known as insulin dependent diabetes mellitus, in this condition, the pancreas does not produce enough insulin according to the ones requirement. This type of diabetes is also called "juvenile onset diabetes mellitus", because it is often diagnosed in children or teenage between 12-18 years. [3]

Type 2 diabetes: - This type of diabetes mellitus is also known as non-insulin dependent diabetes mellitus, this occurs when the body does not produce enough insulin, or when the cells are unable to use insulin properly, which is called insulin resistance. Type 2 diabetes is commonly called "adult onset diabetes mellitus", since it is diagnosed later in life, generally after the age of 45. 90-95% of people are suffering with this type of diabetes.[3]

Other type's diabetes: -

Gestational diabetes occurs during pregnancy and affects about 18 percent of all pregnancies, according to the American Diabetes Association. Gestational diabetes usually goes away after pregnancy, but once you've had gestational diabetes, your chances are higher that it will happen in future pregnancies. In some women pregnancy uncovers Type 1 or Type 2 diabetes and these women will need to continue diabetes treatment after pregnancy.

According to international diabetes federation (IDF), the number of people with diabetes in the world in 2013 was 382 million, which is going to increase to almost 592 million by 2035. India has the dubious distinction of being home to a large number of people suffering from diabetes. According to IDF, 65.1 million of adults in India suffered from diabetes in the year 2013[2]. It has been predicted that the prevalence of diabetes in the adult population in India will be 6% by the year 2025[3].

Diagnosis: -

Diabetes mellitus is characterized by recurrent or persistent high blood sugar, and is diagnosed by demonstrating any one of the following: -

Fasting plasma glucose level [?] (126 mg/dl)

Plasma glucose [?] (200 mg/dl) two hours after a 75-gram oral glucose load as in a glucose tolerance test (OGTT)

Symptoms of high blood sugar and casual plasma glucose [?] (200 mg/dl)

What causes diabetes?

The cause of diabetes is unknown. Genetics, diet, obesity and lack of exercise may play a role in developing diabetes, especially Type 2 diabetes.

What are the symptoms of diabetes?

- Extreme thirst
- Frequent urination
- Blurry vision
- Extreme hunger
- Increased tiredness
- Unusual weight loss

DRUG UTILIZATION REVIEW

Drug utilization review (DUR) is defined as an authorized, structured, ongoing review of prescribing, dispensing and use of medication. It involves a comprehensive review of patients' prescription and medication data before, during and after dispensing to ensure appropriate medication decision-making and positive patient outcomes. As a quality assurance measure, DUR programs provide corrective action, prescriber feedback and further evaluations [5]. . 5 DUR is classified in three categories:

Prospective - evaluation of a patient's drug therapy before medication is dispensed

Concurrent - ongoing monitoring of drug therapy during the course of treatment

Retrospective - review of drug therapy after the patient has received the medication

Drug utilization evaluation is a discipline which aims to understand how and why drug are used as they are, so that drugs use and healthy outcomes can be improved.

Types of Drug utilization review [DUR]:-

Drug utilization studies have also been categorized in to two groups:

Quantitative studies involve the collection, organization and display of estimates or measurements of drug use.

Qualitative studies are multidisciplinary operation, which collect, organize, analyse and report information on actual drug use.

ADR MONITORING/ PHARMACOVIGILANCE

Science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactions (ADRs) or any other medicines related problems.

"ADR is any response to a drug which is noxious and unintended and occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or the modification of physiological function".[6]

AIM AND OBJECTIVE

Primary Objective: To monitor the suspected adverse drug reactions and comparative assessement of Anti-diabetic drugs in diabetic patients at integral institute of medical science and research.

Secondary Objective: Drug utilization pattern of Anti-diabetic drugs prescribed in diabetic patient at integral institute of medical science and research.

STUDY DESIGN

Study design- A prospective observational study.

Study site

Study was carried out in the IPD and OPD of (male and female medicine ward IPD) Integral University Hospital; a 500 bedded teaching hospital situated in the premises of Integral University, Lucknow.

Study duration

The Study was carried out for 6 months.

Study population

Study was conducted on all patients during study period at Integral University Hospital, who had participated; subjects were enrolled on the basis of inclusion and exclusion criteria.

Sources of data

Physician prescribing record

Patient medication profile

Selection of patient

Inclusion Criteria

All the patients were included irrespective of age and sex.

Pregnant and lactating patients were also included.

Exclusion Criteria

- Mentally retarded and unconscious patients.
- Patients who are not treated with drugs.
- Patients unable to comply.
- Drug addicts.

METHODOLOGY

Method and Materials used

Medication Utilization and Adverse Drug Reaction Monitoring (MUADRM) form and CDSCO Suspected ADR Reporting Form. The data was collected in a predesigned format from the medical case sheets, drug charts, and laboratory investigations of 100 patients. The enrolled patients were observed from admission till discharge. Descriptive statistics was applied to the collected data and analyzed using Microsoft Excel software.

Data collection

The following data was collected based on the questionnaire.

- Patient profile (age, sex, weight, patient address, marital status).
- Drugs prescribed (generic/brand name)
- Drugs dose and frequency
- Demographics, current diagnosis, medical history

Evaluation of parameters

The following parameters were evaluated:

Types of antidiabetic prescribed

- Average number of antidiabetic per prescription
- Average age range of patients utilizing antidiabetic
- Comparison of antidiabetic prescribed in monotherapy vs. fixed dose combination therapy
- Comparison of antidiabetic prescribing by generic vs. brand name
- Compliance or adherence (using Weekly Diary Cards).
- A criterion for non-compliance is $< 80\%$ of recommended intake of prescribed drugs.
- Mode of administration of drugs
- Concomitant diseased conditions
- Most commonly used agents of a particular class
- Most common diagnosis
- Average cost of drug per prescription

RESULTS

1. Gender distribution among diabetic patients

Among the 100 diabetic patients, 44 patients were male and 56 patients were female (Figure1)

Gender	No. of Patients	Patients (% age)
Male	44	44%
Female	56	56%
Total	100	100%

Figure 1 : Gender distribution of diabetic patients

2. Age distribution of the study subjects

The lowest numbers of patients were from the age group less than 30 years and the highest percentages were in geriatric patients to 50-60 years (Figure2).

Age (years)	Male	Female	Total no. of patients
Less than 30	**2**	**3**	**5**
30-40	**5**	**8**	**13**
40-50	**11**	**12**	**23**
50-60	**11**	**20**	**31**
60-70	**9**	**12**	**21**
70-80	**6**	**1**	**7**
Total	**44**	**56**	**100**

Table 2: Age distribution amongst diabetic patients

3. Smokers VS non-smokers amongst diabetic patients

38 patients were smokers, in which 24 were males and 14 were females. 62 patients were non smokers including 20 males and 42 females. (Figure3).

Smoking Status	No. of Male	No. of Female	Total
Smokers	**24**	**14**	**38**
Non Smokers	**20**	**42**	**62**
Total	**44**	**56**	**100**

Table 3 : Smokers vs. non-smokers amongst diabetic patients

4. Alcoholics Vs non-alcoholics amongst diabetic patients

It was observed that 2 males and 0 females were alcoholics. Remaining 98 were non-alcoholics including 42 males and 56 were females (Figure 4).

Gender	Alcoholic	Non-alcoholic
Male	02	42
Female	00	56
Total	02	98

Table 4 : Alcoholics Vs non-alcoholics amongst diabetic patients

Type of anti-diabetic prescribed

In this drug utilization study, 100 prescriptions were analyzed. A total of 195 antidiabetic drugs prescribed, of which 37.90 % were Biguanides, 22.60 % sulphonylureas, 25.64 % were insulin. DPP-4 Inhibitors were 7.20% , 1.02% were thiazolidinediones (PPARγ activator) and 5.64% were α-Glucosidase inhibitors. Most of the anti- diabetic prescribed were from the essential medicine list. During the study, it was observed that most frequently prescribed anti-diabetic drug classes were biguanides insulin and sulphonylureas and the most frequently prescribed anti-diabetic as monotherapy among them is Biguanides.

Type of anti-diabetic drug prescribed

Drug class	No. of drugs	Dug (% age)
Insulin	50	25.64%
Biguanides	70	35.90%
Sulphonylurea	48	24.60%
DPP-4 Inhibitors	14	7.20%
Τηιαζολιδινεδιονεσ(ΠΠΑΡγ αχτιατορ)	02	1.02%
α-Γλυχοσιδασε ινηιβιτορς	11	5.64%
Total	195	100%

Type of adverse drug reactions

Overall 9 ADRs were reported during the study (table). hypoglycemia was the most common adr observed in 04 patients (moderate intensity in 2 patients and mild in one patient). Whereas gastric irritation occurs in 02 patients and abdominal discomfort occurs in 03 patients.

Type of ADRs reported

Type of ADRs	No. of Patients	Patients (% age)
Hypoglycemia	04	8.00%

Gastric irritation	02	4.00%
Abdominal discomfort	03	6.00%

Type of gender distribution of ADRs

Overall 9 ADRs were reported during the study, among which 6 patients were males and 3 patients were found to be female. The percentages of ADR distribution among genders were found to be 66.66% in males and 33.33% in females.

DISCUSSION

Little information exists about the perspective behaviour of physicians and the misuse of anti- diabetic drug.

The clinical study i.e.; drug utilization of anti-diabetic drug used in diabetes is carried out for the first time at inpatient and outpatient department of INTEGRAL UNIVRSITY HOSPITAL, LUCKNOW.

In our study, it was observed that over 350 persons (suffering from various diseases) visited the inpatient department of IU Hospital over a period of 6 months. 100 patients, on the basis of inclusion and exclusion criteria, were selected for the present study.

Demographic characteristics showed that percentage of males suffering from diabetes was more than females. It was observed that among them (male and female) 44% were male and 56% were females. Studies showed that females are more persistent diabetic as compared to males; the major reason might be due to the occupational reasons.

Further, it was found that a majority of the patients who were having a diabetes were in the age group of 50-70 years and the lowest % was in less than 30 years of age groups.

In this drug utilization study, 100 prescriptions were analyzed. A total of 195 antidiabetic drugs prescribed, of which 37.90 % were**Biguanides** , 22.60 % **sulphonylureas** , 25.64 % were**insulin** . **DPP-4 Inhibitors** were 7.20%, 1.02% were**τηιαζολιδινεδιονες (ΠΠΑΡγ αςτιατορ)** and 5.64% were**α-Γλυςοσιδασε ινηιβιτορς.** Most of the anti- diabetic prescribed were from the essential medicine list.

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Overall 9 ADRs were reported during the study (table 6.8). Hypoglycemia was the most common ADR observed in 04 patients (moderate intensity in 2 patients and mild in one patient). Whereas gastric irritation occurs in 02 patients and abdominal discomfort occurs in 03 patients, among which 6 patients were males and 3 patients were found to be female. The percentages of ADR distribution among genders were found to be 66.66% in males and 33.33% in females. Among all 9 ADRs, 3 cases of mild (33.33%), 4 cases of moderate (44.44%), and 2 cases of severe (22.22%) types of ADRs were detected.

LIMITATION

Our study have many limitations. The study was carried out over a 6 month period,and the seasonal variations in disease pattern and drug utilization were not considered.

Furthermore, the no of patients was low and the study was restricted only one hospital, hence the result cannot be considered representatives of the whole country. However in spite of all these limitations, our study highlighted some rational prescribing practices. Continuing education on rational drug use and development of easy to use treatment guidelines for common disease suggested. In our future endeavors, we plan to study the effect of regulatory and educational interventions on drug use patterns in the management of diabetes mellitus.

CONCLUSION

The present study was conducted to analyze the rational prescribing of drugs in the medicine ward of a tertiary care hospital using WHO core indicators. Females were more prone to diabetes mellitus.

Metformin , insulin and sulphonylureas was the most commonly used drug. The prescribing trend also appears to be moving towards combination therapy particularly two drugs therapy. This study contributes to the growing body of literature on drug utilization research. However, the study has its own limitations since follow-up of the patients was not possible and hence the effectiveness of the anti-diabetic agents could not be assessed. In the future one can investigate the appropriateness of prescriptions and adherence to evidence based recommendations.

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