

EFFECT OF DRUG THERAPY AND RISK INVOLVED IN CORONARY VASCULAR DISEASE IN TYPE 2 DIABETES MELLITUS - A CASE STUDY

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is one of the chronic diseases in the world. According to World Health Organization (WHO) approximately 171 million people worldwide currently on diabetic and that type 2 diabetes accounts to about 90% . This study presents Oral hypoglycemic agent (OHA) prescription pattern by the physicians among Out patients of two hospital and risk involved in coronary vascular disease (CVD). 160 patients previously diagnosed with T2DM were included in the study, which involves review of available documents, interviewing the patients, their sex, age, smoking habit, family history, Body mass index (BMI), lifestyle, associated disease, Cardiac complication, total no of drugs used, no of drugs prescribed and lastly risk involved in development of the CVD in T2DM. 55% male and 45% female were assessed and subjects above 50 years were found susceptible to Hyperglycemia. Smoking status were- present smokers were 19.4 %, ex-smokers were 33.8%, and non-smokers were 46.8%; family diabetic history - 41.9% had family history, 48.8% were overweight and 10.6% were obese, 55.6 % had sedentary , 28.8% had active and 15.6% had highly active lifestyle. The different group of OHA used were Sulfonylurea 48.9%, Biguanide 41.3% Meglitinide 6.4% and Thiozolidinedione 3.8%. With each class most frequently used drugs were: (a) Sulfonylurea-Glimipiride in 45 patients Glibenclamide in 26 patients Gliclazide in 31 patients Glipizide in 13 patients. (b) Biguanide--Metformin in 98 patients (c) Meglitinide- Repaginide in 15 patients and (d). Thiozolidinedione--Rosiglitazone in 9 patients. The risk factors related to cardiovascular complication like smoking habit, Body Mass Index and Diabetic associated disease was compared. Combination drugs are more effective in controlling blood glucose then that of monotherapy.

Key words: Type 2 Diabetes Mellitus, Overweight, Sedentary Coronary Vascular disease and Combination therapy

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is one of the common chronic diseases in the world^[1]. The prevalence of diabetes T2DM in the Western countries has traditionally been estimated at between 2% to 6%, of which half the patients are diagnosed and similar number unrecognized. However this figure is now known to be much higher in older people and non-white^[2]. The World Health Organization (WHO) estimates that approximately 171 million people worldwide currently have diabetes and that type 2 diabetes accounts for around 90% of these cases^[3]. By the year 2030, the WHO predicts that 366 million people will have this disorder^[4]. Furthermore, even the large numbers of already known people with diabetes may underestimate the true prevalence of T2DM, owing to the existence of a sizeable population of undiagnosed individuals^[5].

Diabetes Mellitus (DM) describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion and action, or both. The effects of diabetes mellitus include long-term damage, dysfunction and failure of various organs ^[6]. The major cause of death in individuals with type 2 diabetes is macrovascular disease (coronary artery, cerebrovascular and peripheral vascular), which accounts for at least two-thirds of T2DM associated mortality ^[7]. In addition, microvascular disease (retinopathy, nephropathy and neuropathy) has substantial impact on the quality of life of individuals with T2DM ^[8]. The WHO concluded that the fasting plasma glucose level diagnostic of diabetes had previously been set too high and recommended that it be lowered from >7.8 mmol/L (or > 140 mg/dL) to >7.0 mmol/L (or > 126 mg/dL) ^[6].

Consequently, strategies for the management of individuals with T2DM should strive to address not only the underlying causes of the disease, but also the complications that arise from it. T2DM begins insidiously and progresses slowly over many years, initially there may be few symptoms and after years of unrecognized disease patients may present with complications of diabetes at diagnosis ^[9]. Genetic factor plays a role with regards to both the insulin resistance and impaired pancreatic β -cells function. However it is well known that environmental factor also plays a major role in the development of the disease these are principally due to high calories intake and limit physical activities ^[10]. Researchers have shown that it is highly advisable to reduce and maintain the blood glucose level to normal due to various complications that arise due to high blood glucose level. For this purpose oral hypoglycemic agents (OHA) are used.

Besides these drug therapies for controlling type 2 diabetes non-pharmacological treatment like lifestyle modification (e.g. physical exercise, low intake of fat, cessation of smoking etc) can decrease and help to control blood glucose in many diabetic patients. These non-pharmacological treatments can enhance the efficacy of OHA and decrease the complication of diabetes and may even reduce the number of drug required including their doses ^[11,12].

Education about the disease is also important in the management of drug therapy and knowledge about the acute and chronic complications is an important factor in achieving the therapeutic goal ^[13].

OBJECTIVES

The objective of this study was to assess the drug use pattern and risk involved in coronary vascular disease (CVD) in T2DM; other objectives were: to assess the drug use pattern in terms of different class and the action of anti diabetic drugs.; to evaluate the risk factors related to T2DM and to evaluate the risk involved in CVD.

MATERIALS AND METHOD

The study was designed as a quantitative, prospective, observational one undertaken during the regular physician visits at the out patients department (OPD) the study was carried out at two different hospitals of Kathmandu valley namely Shahid Gangalal National Heart Center (SGNHC) and Bir Hospital. The study included 160 patients of Type 2 Diabetes Mellitus who were in the range of 30 and above years. Of these, 88 were males and 72 were females and all these patients were previously diagnosed and were receiving Antidiabetic Drugs. (Table 2)

Criteria for the selection:

Inclusion Criteria:

1. Patients with Type 2 Diabetes Mellitus
2. Patients on Oral Hypoglycemic Agents (OHA).
3. Patients with cardiac complication after the diabetes have been diagnosed.

Exclusion Criteria:

1. Patients with Type 1 Diabetes Mellitus
2. The Patients who were on the insulin therapy
3. Patients with any other serious medical illness
4. Patients with pre-hyperglycemic condition, which did not, required medication.
5. Patients with Cardiac Complication before the diabetes have been diagnosed.

Consent of patients were taken by informing them about the research study. Data was collected by developing a structured questionnaire for interview with them and from the patients' present and past history records available.

The questionnaire consisted of particulars of the patients like-name, sex, occupation and education, a medical history-history of diabetes, cardiac complication after the disease had been diagnosed and laboratory investigation consisting of blood glucose level, blood pressure measurement, lipid profile, urine analysis and the questions on the risk factor such as family history, BMI, smoking habit, presence of any associated disease and physical activity. The body mass index was calculated as the weight in kilograms divided by the height in meters squares. Statistical Data Analyses was carried out Using the SPSS 11.0 software chi-square tests were exercise to determine the relationship between drug and patients demographic data and was also for evaluating different variables. Microsoft Excel 2000 was used to draw the graph/figures.

RESULTS AND DISCUSSION

Among 160 patients enrolled in the study, 88 (55%) were male patients and 72 (45%) were female patients. Most of the patients with T2DM were in the age group between 50-59 years (38.8%). Occurrence without family history were found in the greater number than with that of family histories (Table 3). The patients with sedentary (55.6%) life style were more compared to Active (28.8) and highly active patients(15.6%). Out of 160 patients 115 were prescribed with monotherapy. Sulfonylurea-Gliclazide 31 were prescribed, Glimipiride 45 were prescribed, Glibenclamide 26 were prescribed, Glipizide 13 were prescribed. Similarly Biguanide-Metformin 98, Meglitinide- Ripaglinide 15, Thiozolidinedione-Rosiglitazone 9 subject were prescribed (Fig.2). In Combination drug therapy, Glimipiride + Metformin by 33.8% (26) was frequently prescribe (Table 4). Out of 113, controlled blood glucose patients 63 (55.8%) were in the combination therapy and 50 (44.2%) were in the monotherapy and with respect to not controlled blood glucose 33 (70.2%) monotherapy and 14 (29.7%) in combination therapy (Fig.3).

Regarding risk of Cardiac Complication when compared with patients smoking status, it was found that among patients, ex-smokers were more prone in getting cardiac problem (fig.4) Cardiac complication was frequent in obese patients in relation with BMI and cardiac complication 11 (64.7%) (Fig. 5)

Study showed that no disease that is hypertension and hypercholesrolemia has less chances of getting cardiac complication (1,2.5%) (Fig. 6)

Relation between CVD and duration of T2DM shows that chronic disease leads to greater number of occurrence of Cardiac complication (73.9%).

Type 2 Diabetes Mellitus can be defined as a state of absolute or relative insulin deficiency, characterized by hyperglycaemia and the risk of microvascular and macrovascular complications^[15]. Both the WHO and the American Diabetes Association (ADA) recently updated their criteria for the classification and diagnosis of diabetes mellitus^[13,14]. In these, hyperglycaemia remains the defining sign of diabetes. The World Health Organization (WHO) estimates that approximately 171 million people worldwide currently have diabetes and that type 2 diabetes accounts for around 90% of these cases^[3]. By the year 2030, the WHO predicts that 366 million people will have this disorder^[4].

Study was focused in two Hospital of Kathmandu valley and the reason of choosing these hospital was as SGNHC is the specialized hospital for heart and the Bir hospital is the central hospital where patients from different places visit for treatment.

The study showed, increased prevalence of diabetes among male population despite the fact that the risk for developing the disease was similar for both sexes^[15, 16]. However a gender preference of the disease cannot be definitely concluded because the study population was a selected group from two hospitals.

The prevalence of the diabetes was higher in the older age. This is supported by the research work funded by American Diabetes Association Young Investigator Innovation Award in Geriatric Endocrinology^[17] in the University of Michigan. The result corroborated our hypothesis that age was one of the risk factor of T2DM. The incidence of diabetes in the patients with second-degree family history was less common and the more number of patients were with no family history. This was due to the urbanisation and life style changes^[18] Study shows that there is strong relation between the sedentary lifestyle and diabetic conditions. Greater the sedentary life style, greater was the chances of getting diabetes. The American Diabetes Association Clinical Practice Recommendations 2001 says " the possible benefits of the exercise in the T2DM are substantial." These guidelines refer mainly to glycaemic control.

Sulfonylurea urea and more given drugs, in this class Gimipiride in most prescribed one, this is support by the study made by Stephen N. Davis^[19] in 2004, Tomoya Hamguchi in 2004^[20]

Metformin was the choice of drugs for the obese patients and it produced fewer side effects in comparison with other sulfonylurea group. The agent target organ was the liver and the risk of hypoglycaemia was eliminated when used mono therapy^[21]. Where as Rosiglitazone and Ripaglinide and newly introduced drugs in the market; therefore for use of this drug was comparatively lesser than other OHA. Easy availability; physicians prescribing trend or heavy promotional approaches of the drug by the manufacturer could be some other factors.

Metformin was used in all the case in combination with other classes of drugs as it produced fewer side effects. This may also be because of easy availability, physicians prescribing trend and heavy promotion of the drug by the manufacturer.

The results showed that higher proportion of the subjects with the controlled blood glucose were on the combination therapy. Thus we can infer that blood glucose can be controlled

more effectively by the combination therapy. In other words combination drug therapies are more effective in diabetes than monotherapy.

The study showed that prevalence of cardiac problem increased with the smoking in diabetic patients supported by American Diabetes Association survey made in 1998^[46] which showed that induces smoking increase the amount of cholesterol in the blood resulting in CVD^[20, 21]

The patients with over weight are prone to cardiac complication as fasting hyperinsulinemia, increase apolipoproteins B concentration and increase proportion of small dense, low lipoproteins, - was found to be associated^[22] with 20 fold increase in risk of developing CVD^[22]

The results showed that there was a strong relation between the cardiac complication and Diabetic associated disease. The finding was supported the study made by S.M Marshall, which indicated that In his research he found that there is the strong relation between these factors^[49]. In dyslipidaemia LDL level in the diabetes patients are 4 times greater in case of diabetes when Triglyceride level increase, activity of factors VII and X are increased as are platelets level leading to CVD.^[23]

In hypertension sympathetic activity may cause release catecholamine results in increase blood pressure, and leads to increase volume retention of sodium resulting in increase in blood pressure.^[23]

The results showed that there was increased prevalence among males than females and this results is supported by different studies^[24, 25]. Thus it is concluded that male and female sex are not equally prone to the cardiovascular complications.

The results show that as the duration of the disease is increases there were more chances of getting CVD due to many other risk factors involved and the involvement of different associated disease this is supported by the different studies^[25, 26]

CONCLUSIONS

Increase prevalence of T2DM occurs over the age 50. BMI, smoking habit, sedentary lifestyle and other associated disease have negative correlation with insulin sensitivity, resulting in CVD. The study shows that the most frequently used drugs are of class Sulfonylurea and Biguanide in that most used was Glimipiride and Metformin respectively. Combination therapy was more effective in controlling blood glucose than monotherapy. Chronic patients are likely to get cardiovascular complication. Males are more prone to CVD than compared to females.

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Table-1

Category	BMI*
Underweight	<18.5
Normal	18.5-24.9
Overweight	25.0-29.9
Obese	>30.0

*BMI: National Institutes of Health, 1998

Table-2

OHA	On. of patients	Percentage
Sulfonylurea	115	48.5
Biguanide	115	48.5
Meglitinide	98	44.3
Thiazolidinediones	15	6.4
	9	3.8

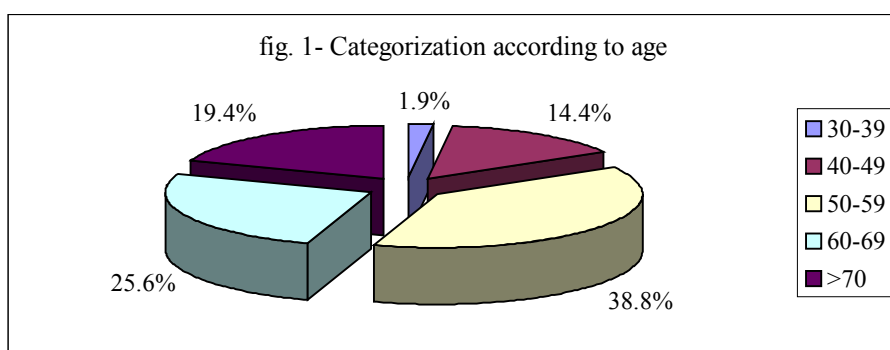


Table 3 Distribution of diabetic patients according to family history

Family History	No. Of patients	Percentage (%)
First-degree	50	31.2
Second-degree	3	1.9
Both	14	8.8
No history	93	58.1
Total	67	41.9

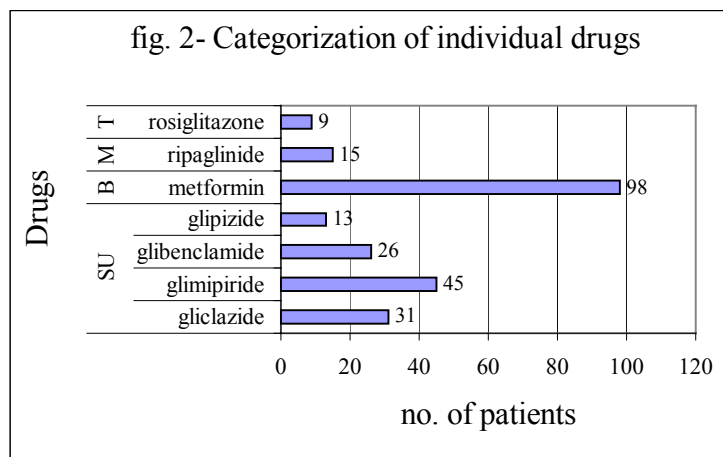
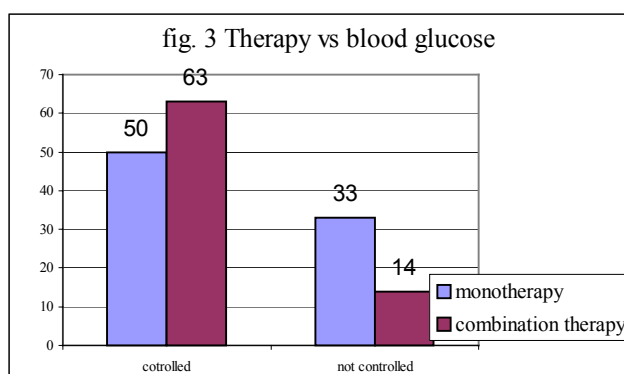
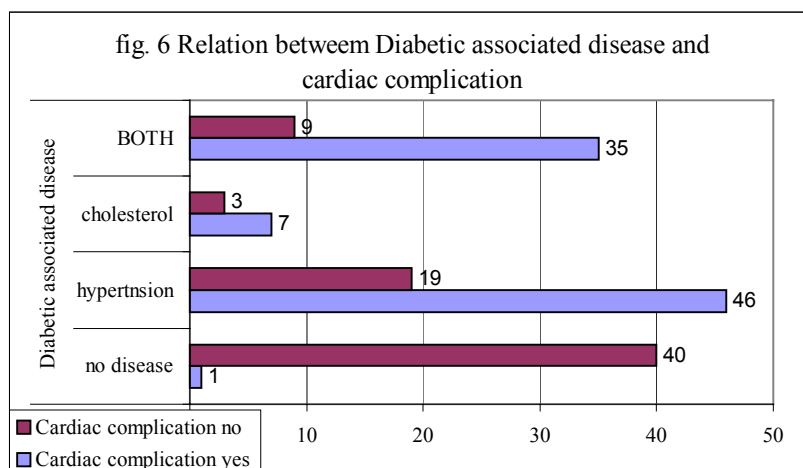
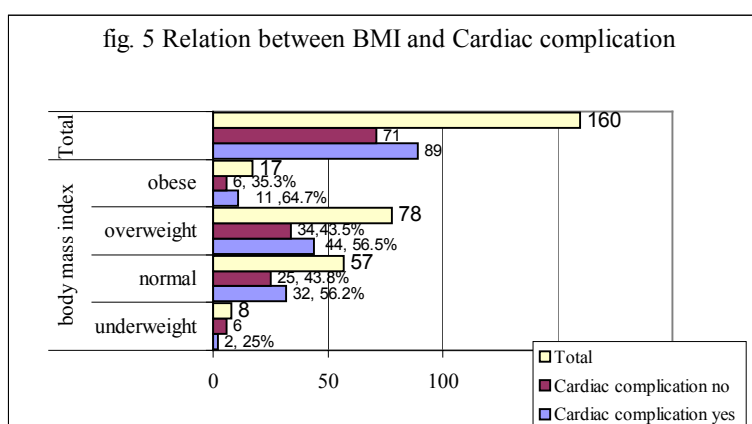
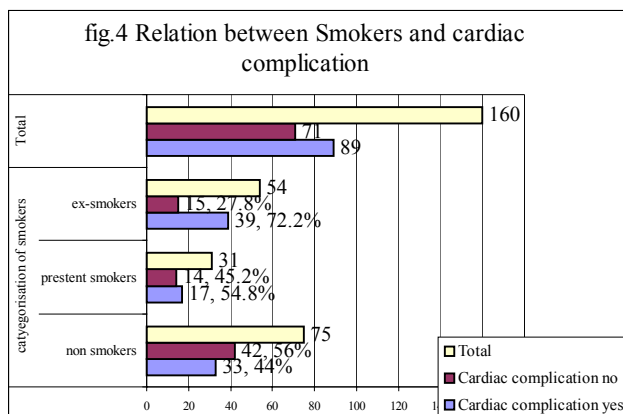


Table 4 Distribution of number of patients (%) administered combination therapy

Combination drugs	No. of patients	Percentage
Glimipiride +metformin	26	33.8
Glibenclamide +metformin	18	23.4
gliclazide +metformin	18	23.4
rosiglitazone +metformin	5	6.4
repaglinide +metformin	4	5.2
glypizide +metformin	6	7.8





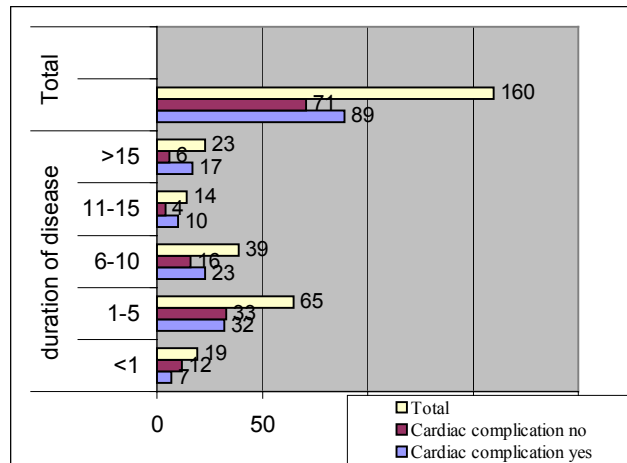


Fig.7 relation between CVD and duration of T2DM