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RESEARCH ARTICLE

CAUSES OF HYPOGLYCEMIA IN ADULT PATIENTS WITH TYPE 2 DIABETES MELLITUS IN A TERTIARY HOSPITAL

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ABSTRACT

Background: Hypoglycemia is a common medical emergency in diabetic patients, which is defined biochemically with blood glucose level 45-50 mg/dl with clinical features of adrenal over activity and neuroglycopenia. It is one of the preventable acute complications of diabetes mellitus through appropriate outpatient diabetes management. Our study aims to find out the causes of hypoglycemia in the patients with type-2 diabetes in a tertiary care hospital.

Methods: This cross sectional observational study was performed in BIRDEM General Hospital on 100 adult type 2 diabetic hypoglycemic patients of both sexes to find out causes of hypoglycemia. and to determine the knowledge of overall diabetic education including dietary compliance (regular meal timing, consistency of day- to- day intake, meal spacing, sucrose limitation, calorie restriction and food exchange system etc), recommended way of exercise (aerobic, anaerobic, with complications etc.) and sick day management. Alterations of common biochemical parameters and presence of concomitant diseases in patients with hypoglycemia were studied.

Results: Hypoglycemia occurred more in elderly (56%), with long duration of DM (56%) and frequency slightly more in male (66%) than female**.** Fifty percent of the patients presented with clinical features of severe hypoglycemia. Delay or omission of a snack or meal alone was the commonest (53%) cause in this study. Delay or omission of a snack or meal plus irregular diet habit emerged as 2nd important cause (22%). In 11% cases irregular dietary habit alone was responsible, and administration of excess insulin/secretagogues were responsible in only 4% cases. Hypertension (66%) was the most prevailing co-morbid condition. Others were nephropathy (38%), IHD (30%), diabetic neuropathy (19%), diabetic retinopathy (17%), dyslipidemia (12%), stroke (9%) and PVD (2%). Most of the hypoglycemic patients (69%) were on insulin when they had spells of hypoglycemia. The glycemic status was poor in most (87%) cases, having HbA_{1c}>7%. Regarding overall diabetes care only 7% had some knowledge about diabetic education.

Conclusion: In the present study, delay or omission of meal and irregular dietary habit were the causes of hypoglycemia in most of the cases, which signify lack of proper diabetic health education. Therefore, diabetic self management education is the most important element for the prevention of hypoglycemic events, and also to prevent long-term complications.

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INTRODUCTION

Hypoglycemia is a common medical emergency in diabetic patients, which still remains the main barrier for tight blood glucose control.

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The laboratory diagnosis of hypoglycemia is usually defined as a plasma glucose level <2.5–2.8 mmol/L (<45–50 mg/dL), although the absolute glucose level at which symptoms occur varies among individuals (Cappola, 2009). If above definition of hypoglycemia is applied, the frequency in unselected population of insulin treated diabetic patients ranges from 0.2-1.6 episodes/patient/year (Cryer, 2001). Hypoglycemic individual may show either mild attack, which is self treated

with oral carbohydrate or severe attack when the patient needs assistance or intervention of others for recovery. Severe hypoglycemia does not require the development of coma or convulsion. Profound neuroglycopenia can occur without loss of consciousness and is manifested as overt cognitive dysfunction (Cryer, 2001). As the evidence emerged that tight metabolic control reduces risk of micro vascular complications, early attempt to maintain near normal glucose level may lead to frequent and severe hypoglycemic episodes as found in the Diabetes Control and Complications Trial (DCCT) (The Diabetes Control and Complications Trial Research Group, 1993). Therefore, hypoglycemia remains one of the most important barriers for achieving tight glycemic control. Bangladesh is a developing country which cannot bear the huge cost related to the more common acute complications of diabetes especially hypoglycemia. Prolonged and repeated hospitalization may be needed for the management of hypoglycemia. So it is justified to find out the causes to prevent hypoglycemia rather than its management. This justifies this study to be done on patients admitted into hospital due to hypoglycemia. The risk of hypoglycemia can be reduced by frequent and appropriate blood glucose monitoring, self adjustment of insulin dose and oral hypoglycemic agents, use of proper delivery device and delivery techniques, self adjustment of food during illness and exercise, good patient compliance and appropriate management of risk factors.

Objectives of the study

General Objective:

To find out causes of hypoglycemia of adult type 2 diabetic patients attending in a tertiary care hospital (BIRDEM).

Specific Objectives:

- To determine the knowledge of overall diabetic education in type 2 diabetic patients in our population.
- To find out relation of hypoglycemia with concomitant diseases.
- To find out alteration of common biochemical parameters in patient with hypoglycemia.

MATERIALS AND METHODS

This was a cross sectional observational study conducted from April, 2010 to September, 2010 to find out causes of hypoglycemia of adult type 2 diabetic patients admitted in a tertiary hospital (BIRDEM). Study subjects were selected from medicine in-patient department of BIRDEM General hospital, Dhaka by purposive sampling.

Selection criteria

The inclusion criteria was- Diagnosed type 2 diabetic patients of both sexes admitted into hospital with symptoms of hypoglycemia and capillary blood glucose less than or equal to 2.8 mmol/L and age ≥18 years. The criteria of exclusion included- Diabetic patients aged less than 18 years, patient developing hypoglycemia after admission into hospital, non-diabetic patient, patient with psychiatric illness, patient suffering from DM other than type 2 and those who did not give consent for the study. Hypoglycemia was defined as venous blood glucose to a low a level varying from 2.5 to 2.8 mmol/L (45-50mg/dl) with or without clinical features (Cappola, 2009). Sample size was calculated considering 10% margin of error and a prevalence of 70% (Briscoe *et al* 2006) based on the cross sectional sample size determination formula [n = (z2pq/d2)]. The required sample size was 164. But due to time and resource constraints, data was collected from 100 patients.

Data collection procedure

Total 100 adult type 2 diabetic patients (20 to 79 years) were selected in this study according to selection criteria. They were selected purposively from inpatient department of Medicine, BIRDEM. The purpose of the study was explained to each subject in detail. After primary selection a detailed clinical history was taken and physical examination was done. Severity of hypoglycemia was assessed. The relevant biochemical tests were performed and results recorded. The data were collected in a pre-formed standard printed data collection form after taking written informed consent of the patient. Data collection forms were filled in at hospital at bed side each time. Permission from ethical review committee of diabetic association of Bangladesh had been obtained. The collected data were analysed using SPSS version 16.

RESULTS

Most of the study subject were male (66%). Elderly people of the age group 51-70 years consisted 56% of the study subjects. Next to them were from age group of 31-50 years (23%). The lowest number of subjects belonged in the age below 30 years. Most of the subjects (59%) had normal BMI (within 18.5-22.9 Kg/m^2). Obese subjects were 26%. Only 7% of the subjects were underweight and rest (8%) were overweight. Most important causes of hypoglycemia in this study were delay or omission of a snack or meal (53%), combined (delay or omission of a snack or meal and irregular diet habit), (22%) and irregular dietary habit (11%). Others were self administration excess insulin/secretagogues (4%), mismatched

Table 1. Causes of Hypoglycemia among the respondents (N=100)

Causes of hypoglycemia	Frequency	Percent	Cumulative Percent
Delay or omission of a snack or Meal	53	53.0	53.0
Self administration of excess insulin/secretagogues	4	4.0	4.0
Mismatched insulin &syringe	2	2.0	2.0
Maladjustment of doses of insulin/secretagogues	2	2.0	2.0
Irregular diet habit	11	11.0	11.0
Delay or omission of a snack or meal + Irregular diet habit	22	22.0	22.0
Delay or omission of a snack or meal +Maladjustment of doses of insulin/ secretagogues	4	4.0	4.0
Delay or omission of a snack or meal + Adrenal insufficiency	2	2.0	2.0
Total	100	100.0	100.0

insulin & syringe (2%), maladjustment of doses of insulin/ secretagogues (2%), delay or omission of a snack or meal plus maladjustment of doses of insulin/ secretagogues (2%) and delay or omission of a snack or meal plus adrenal insufficiency (2%) (Table 1). Most of hypoglycemic patient (69%) took insulin as antidiabetic medication when they had spells of hypoglycemia. Moreover 10% patients took both OAD and insulin as medicine and rest (21%) took only OHA. Among the study subjects using insulin, 49% were on premixed insulin (96% on 30/70 and 4% on 50/50 formulation), 14% short acting insulin only, 9% on split mixed regime, and 7 % on intermediate acting insulin only, during the hypoglycemic events. Among the 100 hypoglycemic subjects, 56% had have diabetes for the duration of 10 to 20 years. Among the rest, 18% and 17% subjects had have diabetes for the duration of less than 5 years and 5-9 years respectively. Rest had diabetes for 21 years or more (Table-2).

Table 2. Duration of diabetes of the hypoglycemic patients (N=100)

Duration of diabetes in Years	Frequency	Percent
Less than 5	18	18.0
5-9	17	17.0
10-20	56	56.0
Above 21	9	9.0
Total	100	100.0

In this study the majority of the hypoglycemic patients had associated co-morbid diseases. Hypertension (66%) was the most prevailing co-morbid condition. Others were nephropathy (38%), diabetic neuropathy (19%), diabetic retinopathy (17%), IHD (30%), dyslipidemia (12%), stroke (9%) and PVD (2%). Among the subjects 11% had no co-morbid condition (Table-3). Most of the hypoglycemic events (50%) were of severe category required hospital admission with prolonged and intensive medical care. Level of education regarding overall diabetes care particularly regarding hypoglycemia was very poor among the study subjects. Only 7% of them had some knowledge about diabetic education. However in rest (93%) of the cases, level of education was very poor (Table 4). Regarding dietary modification 5% had sufficient sick day management and 2% had porper knowledge about exercise.

Table 3. Distribution of hypoglycemia by relationship of associated illness (N=100)

Associated illness	Male	Female	Percent
Retinopathy	11	06	17.0
Neuropathy	13	06	19.0
Nephropathy	21	17	38.0
HTN	46	22	66.0
PVD	02	0	2.0
Dyslipidemia	08	04	12.0
IHD	24	06	30.0
Stroke	06	03	9.0

DISCUSSION

The conventional risk factors for iatrogenic hypoglycaemia, conceptualised in Type 2 diabetes but relevant to Type 2 diabetes, are based on the premise that absolute or relative insulin excess, whether injected or secreted insulin, is the sole determinant of risk. Absolute or relative insulin excess occurs when insulin, or insulin secretagogue or sensitizer, doses are excessive, ill-timed or of the wrong type; exogenous glucose delivery is decreased after missed meals or snacks and during the overnight fast; endogenous glucose production is decreased after alcohol ingestion; glucose utilization is increased during exercise; sensitivity to insulin is increased late after exercise, in the middle of the night and after weight loss, increased fitness or improved glycaemic control or during treatment with an insulin sensitizer; insulin clearance is decreased as in renal failure (Cryer *et al*., 2002).

Table 4. Extent of the Diabetic education among the hypoglycemic patients (N=100)

Status of the diabetic education	Frequency	Percent
Knowledge about dietary modification	05	5.0
Knowledge about way of exercise	02	2.0
Knowledge about sick day management	00	0.0

Table 5. Biochemical parameters among study subjects (N=100)

Biochemical parameter	Category	Percent of study subjects.
HbA1c	<7%	13%
	7%-10%	50%
	>10%	37%
Serum Creatinine (mg/dl)	<0.68	20%
	0.68-1.2	66%
	>1.2	14%
SGOT (IU/L)	<37	95%
	≥37	5%
SGPT (IU/L)	<40	83%
	≥40	13%
HDL (mg/dl)	<40	69%
	>40	31%
LDL (mg/dl)	<100	94%
	≥100	6%
TG (mg/dl)	<150	59%
	≥150	41%

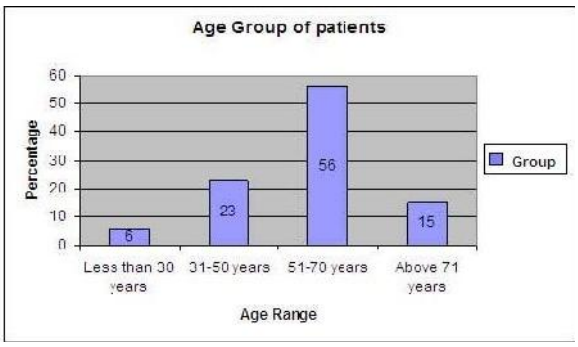

Figure 1. Age distribution of the hypoglycemic patients (N=100)

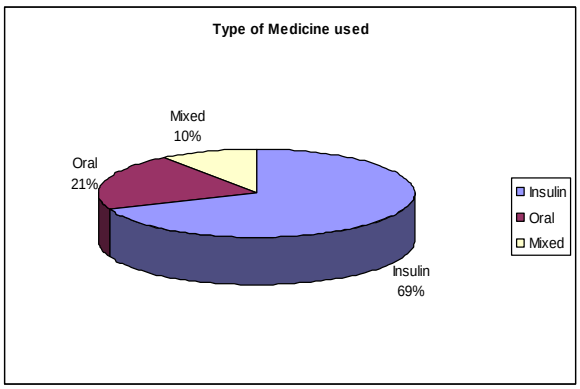

Figure 2. Types of medicine causing hypoglycemia among the cases (N=100)

In this study, delay or omission of a snack or meal was the commonest (53%) cause, followed by other causes like delay

or omission of a snack or meal plus irregular diet habit. However, other important risk factors that act as clinical surrogates of compromised glucose counterregulation (eg. absolute insulin deficiency, aggressive glycemic goals etc.) were not addressed in our study. Insulin can produce absolute or relative insulin excess largely because of dosing and pharmacokinetics. With a basal-bolus insulin regimen, morning fasting hypoglycemia implicates the long-or intermediate-acting insulin. Daytime hypoglycemia may be caused by the rapid-, short-, or longer-acting insulins, depending on the regimen. Nocturnal hypoglycemia may also be caused by regular and longer-acting insulin. Insulin secretagogues, eg.sulfonylureas, repaglinide, and nateglinide—can also produce hypoglycemia related to absolute or relative insulin excess. However, the sulfonylureas may pose the greatest risk of hypoglycemia in patients with altered renal or hepatic function and in older adults. Hence, agents such as glimepiride, glipizide XL, or nateglinide that are shorter-acting and have glucose-dependent insulin secretion would be preferable to reduce hypoglycemic risks (Cryer, 2001). In this study population most of hypoglycemic patient took insulin as medicine when they had spells of hypoglycemia. Moreover 10% patients took both OHA and insulin as medicine and rest took only OHA. During the hypoglycemic events, 49% of the insulin using study subjects were using premixed insulin.

Education regarding all aspects of diabetes care is important in the prevention and treatment of hypoglycemia. Carbohydrate counting, insulin and oral medication dosing, concomitant medications, alcohol intake, exercise, and even driving should be included in the discussion. Education will help alleviate fear of hypoglycemia that may impede ideal glycemic control. Reducing hypoglycemia will involve patient empowerment and anticipatory guidance by both patients and health care providers. Providers will also take on the role of facilitator as they help patients navigate through the maze of diabetes self-care. Lack of understanding of the diabetes-related therapeutic regimen will contribute to repeated incidents of hypoglycemia. Patients must understand time action profiles of their diabetes medications and realize that excessive treatment can be harmful. Providers should urge patients to wear potentially lifesaving diabetes alert identification. Blood glucose monitoring is fundamentally important for people who experience hypoglycemic episodes, especially before they perform critical tasks such as driving (The Diabetes Control and Complications Trial Research Group, 1993). In this study, level of education among study subjects regarding overall diabetes care particularly regarding hypoglycemia were very poor among the study subjects (93%).

Older individuals with diabetes who have co-morbidities such as dementia, cerebral vascular accident, or depression, consideration should be given to these confounding factors (United Kingdom Prospective Diabetes Study Group, 1995). In this study the majority of the hypoglycemic patients had associated co-morbid diseases. Hypertension was the most prevailing co-morbid condition. Others were nephropathy, diabetic neuropathy, diabetic retinopathy, IHD, dyslipidemia, stroke and PVD. Most of the hypoglycemic events (50%) were of severe category requireing prolonged and intensive medical care. Elderly are at increased risk for hypoglycemic coma (The Diabetes Control and Complications Trial Research Group, 1993) and they have reduced awareness of the autonomoic symptoms of hypoglycemia. In this study, most of the study subjects were elderly (56%).

Limitations of the study

The short duration of the study may have limited the ability of the study to find out the causes of hypoglycemia. Due to time and financial constraints, follow- up could not be carried out. Incidence and prevalence rates of hypoglycemia could not be estimated as the study was carried out in only one center and had a small sample size.

Recommendations

On the basis of the results of the present study, recommendations are

- Doctor and other healthcare providers should take the role of facilitator as they help patients navigate through the maze of diabetes self-care.
- Routine blood glucose monitoring should be done.
- Hypoglycemia is problematic in advanced type 2 diabetes because of compromised glucose counter-regulatory systems.

Therefore, education concerning self-monitoring of blood glucose, diet, physiological insulin replacement, medication, and lifestyle are important to maintain good glycemic control, avoid hypoglycemia, and prevent long-term complications.

Conclusion

The present study demonstrates that the most important factors associated with hypoglycemia in this cross sectional population were delay or omission of a snack or meal, irregular diet habit, older age and increased duration of diabetes. Premixed insulin was the most common medication causing hypoglycemia, followed by oral hypoglycemic agents. It also shows the poor level of education regarding diabetes, particularly regarding hypoglycemia among the study subjects. Adequate steps to minimize these factors may help to reduce the burden of hypoglycemia, and therefore the overall burden of the treatment of diabetes in our country.

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