Original Article

Clinical Evaluation of Predisposing Factors of Hypoglycaemia in Diabetic Patients

Mohammad Motiur Rahman,[1] Suzauddin Talukder,[2] Issa Muhammad Baker,[3] Anupam Das,[4] Md. Abdul Baset,[5] Farjana Najnin [6]

Abstract

Background: Hypoglycemia is a common medical problem in diabetic patients, and the potential range of morbidity and mortality in diabetic patients exposed to hypoglycemia is significant. The study was conducted to evaluate the predisposing factors of hypoglycemia in diabetic populations.

Methods: This is a descriptive cross-sectional study carried out in the indoor and outdoor patient department of BIRDEM hospital, Dhaka, Bangladesh, from July 2009 to December 2009 after ethical approval in conformity with the revised 1964 Helsinki declaration. Following informed written consent, a total of 50 diabetic patients having hypoglycemia were finally included. Data analysis was done using SPSS 17.

Results: In the study population, significant members of hypoglycemic episodes were found in middle age (31-70) insulin-treated patients and poor diabetic education and in those who had other concomitant diseases. Poor dietary compliance (Reduced meal intake in 50% of cases and missed meal in 34% of cases) and lack of proper diabetic education about early recognition and treatment of hypoglycemia also appeared as important contributory factors. Noncompliance with regular exercise (40%) and unaccustomed exercise (4%) contribute to hypoglycemia. A significant number of hypoglycemic patients have chronic renal insufficiency (68%).

Conclusion: Hypoglycemia is common in the diabetic population who have poor knowledge and practice about diet, drug exercise technique of, use of insulin devices, and have an underlying systemic illness. So more rational education system and appropriate management of systemic diseases regarding the prevention and treatment of hypoglycemia is demanded by our diabetic patients.

Keywords: Hypoglycaemia, Diabetes mellitus, Diabetes hypoglycemia, hyperinsulinaemic hypoglycemia

Introduction

Hypoglycemia is a common medical emergency in diabetic patients, which remains the main barrier to tight blood glucose control.[1] Severe hypoglycemia within a single year affects between 10% and 30% of a diabetic population.[2] The glycemic thresholds for symptoms of hypoglycemia are dynamic and may alter due to repeated exposure to hypoglycemia and hyperglycemia. However, many patients appear to

[1] Junior Consultant, Medicine, Upazilla Health Complex, Puthia, Rajshahi.
[2] Junior Consultant (Medicine), Upazilla Health Complex, Basail, Tangail.
[3] Junior Consultant (Medicine), National Institute of Neurosciences and Hospital, Dhaka
[4] Medical Officer, Mugda Medical College Hospital, Dhaka.
[5] Junior Consultant (Medicine), Upazilla Health Complex, Poba, Rajshahi.
[6] Junior Consultant (Obs & Gynae), Upazilla Health Complex, Puthia, Rajshahi.

tolerate relatively low blood glucose concentration without demonstrable symptoms, while others (particularly if their diabetes is poorly controlled) may develop florid symptoms of hypoglycemia when blood glucose falls within the normal range.[3]

In human, the initial response to a decline in blood glucose is suppression of endogenous insulin secretion followed by the release of counterregulatory hormones, of which glucagon and epinephrine (adrenaline) is the most potent.[4] Therefore, subjective recognition of the symptoms of hypoglycemia is fundamental to effective self-management and preventing progression in severity. With increasing age, the symptoms of hypoglycemia may become less intense, and the symptom profile is modified, most probably due to a decreased response of counterregulatory hormones.

Frequently medically ill patients have multiple reasons for developing hypoglycemia, including renal failure, hepatic dysfunction, sepsis medications, and poor dietary intake. Hepatic failures lead to hypoglycemia because of the liver's role in gluconeogenesis, glycogenolysis, and poor dietary intake. The hypoglycemia of congestive heart failure, sepsis, and lactic acidosis is likely due to hepatic dysfunction. Hypoglycemia occurs with adrenal insufficiency but is uncommon. Starvation states, such as anorexia nervosa and protein-calorie malnutrition, also cause hypoglycemia.

Despite facilities of Home Monitoring of Blood Glucose (HMBG) invention of newer antidiabetic drugs and insulin with less hypoglycemic potential, the incidence of hypoglycemia is still high. So, it is justified to find out the predisposing factors to prevent hypoglycemia rather than its management.[5] 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 the proper device and delivery techniques, self-adjustment of food during illness and exercise, good patient compliance, and by appropriate management of risk factors.

The diabetes control and complication trial (DCCT) group[6] has shown that improved glycemic control is associated with sustained decrees of microangiopathy, which is the major cause of both morbidity and mortality in diabetic patients. Bangladesh is a developing country that cannot bear the huge cost related to the complication of diabetes. Prolonged and repeated hospitalization may be needed for the management of complications of diabetes. So, every diabetic patient needs targeted diabetic control, which needs good diabetic knowledge & practice, preferably by self-monitoring of the diseases the patient himself.

This study was designed to evaluate the common predisposing factors of hypoglycemia in diabetic patients and determine the relationship between dietary compliance, diabetic educational status, and concomitant diseases with hypoglycemia.

Materials and Methods

Study design, study site, and selection of the patients: This hospital-based cross-sectional study was conducted in the In-patient and outpatient department of Endocrine Medicine, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Bangladesh, from July 2009 to December 2009. Formal ethical approval was taken from the Institutional Review Board (IRB) of BIRDEM. After describing the aim, purpose, and procedure of the study, a total of 50 diabetic patients having random capillary blood glucose less than 45 mg(2.5mmol/L) or developing hypoglycemia after admission into the hospital were finally enrolled. Informed written consent was taken from each participant. Detailed history and thorough clinical examinations were performed for each patient to obtain maximum clinical information with a view to evaluating predisposing factors of hypoglycemia. All the cases were investigated by Random capillary blood glucose, HbA1c (by HPLC-based HbA1c analyzer), serum creatinine (by sodium picrate method/Jaffe method), S. bilirubin and SGPT (enzymatic colorimetric method).

Data collection methods: Data were collected either from patients or their attendants through direct interviews with a semi-structured questionnaire. All collected data were recorded in a structured case record form and later accumulated and compiled.

Ethical statement: All procedures performed in studies involving human participants were in accordance with the institutional (BIRDEM) ethical standards and with the 1964 Helsinki declaration and its later amendments or

comparable ethical standards. For this type of study, formal consent was ensured. Furthermore, ethical measures were taken throughout the study period to maintain a high standard of confidentiality and anonymity of the participants.

Data acquisition and statistical analysis: All data were entered, checked & scrutinized by the principal investigator following standard procedure. Data were analyzed by SPSS (statistical package for social science), version 17.

Results

Among 50 hypoglycemic patients, the maximum number was in the age group 51-70 (80%) years and the age group of more than 31-50 (16%). The lowest number of patients belonged to the age group of less than 30 (4%). Maximum study patients were female (56%). In this study, 60% of patients were found to have improper timing of meals, and 40 patients were found to have meals at fixed times. Among all the subjects, only 40% of patients were found to do regular exercise, whereas 60% of patients were not doing regular exercise. Two patients (4%) were found to have been unaccustomed to exercise without modification of diet and drug before hypoglycemia, while the rest of the 96% of patients had no history of unaccustomed exercise. The most frequent number of patients was found taking insulin (62%), then oral hypoglycemic drug (30%), and insulin plus oral hypoglycemic drug (8%). Most of the patients in this study had HbA$_1$C between 7-10%, 12% had HbA$_1$C levels less than 7%, and 24% had HbA$_1$C more than 10%. In this study, 68% have an abnormal renal function, whereas 32% have normal renal function. [Table 1]

In this study, 90% of patients know about hypoglycemia, 86% know the home management of hypoglycemia, 80% know the hypoglycemia symptom, 66% know the insulin injection technique, 18% of the patients could monitor blood glucose, and 14% of patients could adjust insulin. Among all the subjects, only 32 % subject was followed dietary advice. Half of the study patients (50%) were found to have reduced meals before hypoglycemia, whereas 34% had a history of missed meals, and 8% of patients had a history of vomiting before hypoglycemia. [Table 2]

Table 1: Sociodemographic profile of the participants (n=50)

Variables	n (%)
Age (years)	
51-70	40 (80)
31-50	8 (16)
≤30	2 (4)
Gender	
Male	22 (44)
Female	28 (56)
Meal time	
Fixed	20 (40)
Not fixed	30 (60)
Exercise*	
Regular	20 (40)
Irregular	30 (60)
Unaccustomed exercise without modification of diet and drug	2 (4)
DM treatment	
Insulin	31 (62)
Oral hypoglycaemic agents (OHA)	15 (30)
Insulin plus OHA	4 (8%)
HbA1c status	
Below 7%	6 (12)
7.1% to 10%	32 (64)
More than 10%	12 (24)
Renal function	
Normal	16 (32)
Abnormal	34 (68)

*Multiple responses considered

Table 2: Diabetic education and dietary compliance of the participants (n=50)

Variables	n (%)
Diabetic education status	
What is hypoglycemia	45 (90)
Home management of hypoglycemia	43 (86)
Symptoms of hypoglycemia	40 (80)
Insulin injection technique	33 (66)
Monitor blood sugar	9 (18)
Adjust insulin	7 (14)
Dietary compliance	
Meal reduction before hypoglycemia	25 (50)
Meal missed before hypoglycemia	17 (34)
Vomiting occurred before hypoglycemia	4 (8)
Dietary advice	
Followed	16 (32)
Not followed	34 (68)

Discussion

Diabetes and its complications are the major cause of morbidity[7] and mortality[8] throughout the world. Hypoglycemia is one of the most important complications of diabetes. The frequency of hypoglycemia in an unselected population of insulin-treated diabetic patients ranges from 0.2 – 1.6 episodes /patient/year, according to the data suggested. Regarding the clinical presentation of hypoglycemia in this study, it was observed that 38 (76%) patients presented at the age between 1 to 70 years, which is the typical age for diabetes mellitus.

The study was undertaken to address several clinical questions to discover the magnitude of the problem of hypoglycemia in the hospital setting and determine the distribution of cases according to cause. There is various risk factor that predisposes to hypoglycemia in diabetic patients. This includes decreased intake of meals or missing meals despite taking antidiabetic drugs, maladjustment of antidiabetic drugs during illness and exercise due to lack of proper diabetic education and practice, the incorrect technique of use of devices, improper timing of use of drugs, and systemic discuses.

In this study, half of the population was found to have a history of reduced meals, and 1/3rd of patients were found to have missed meals before hypoglycemia. As normalization of blood glucose is associated with an increased risk of hypoglycemia, comprehensive evaluation of diabetic education is very much essential in recognition of symptoms of hypoglycemia and its prevention and management.[9] A previous study conducted in 2005 has described that only 5-7% of the study population bed knowledge about hypoglycemia.[10] However, this study found that a maximum number of patients have knowledge about hypoglycemia, insulin injection technique, and home management of hypoglycemia. This may be due to the increasing awareness among diabetic patients and various diabetic education programs conducted by the Bangladesh Diabetic Society throughout the country. According to the

position statement of the American diabetic association (ADA), self-monitoring of blood glucose is considered an important component of diabetes care and is recommended for all insulin-treated patients.[11] In our study, a history of home monitoring of blood glucose was found only in 18% of patients, which is very much low in comparison to 95% of users of HMBG in Italy.[12]

In the present study, maximum Hypoglycemic patients were preserved with a history of insulin treatment. In the UKPDS study, three intensive treatments were compared by actual therapy; major hypoglycemic or any episodes were most common in patients of insulin therapy.[13]

After looking at the distribution of hypoglycemia with HbA_1C, we found that almost $2/3^{rd}$ patients had HbA_1C between 7-10%, which is higher than the normal reference value. On the other hand, only 12% of patients had normal HbA_1C, which is very dissimilar to the study carried out by DCCT, where severe hypoglycemia was inversely correlated with mean HbA_1C[6]. The dissimilar finding was due to the recruitment of many study subjects who had uncontrolled blood sugar during the presentation with hypoglycemia and had a history of poor diabetic education and practice regarding their diet, drug, and exercise.

A significant number of cases of hypoglycemia were related to renal insufficiency in our study population. A similar significant contribution was also found in a study of hypoglycemia in hospitalized hypoglycemic patients carried out by Kathleen F and Fisker MD, were 20 diabetic patients with hypoglycemia out of 94 hypoglycemic individuals had associated renal insufficiency. In renal failure, several mechanisms for the development of hypoglycemia have been proposed, including poor dietary compliance and reduced renal glucose production. The pathogenesis of hypoglycemia in real insufficiency is a complex problem deserving further investigation, mainly because the incidence of this problem is much higher. A study carried out by Kathleen F, and Fisher MD on hypoglycemia in the hospitalized patient showed that out of 42 diabetic patients admitted to the hospital with hypoglycemia, eight patients had no identifiable cause of hypoglycemia.[14]

Limitations

The study has several limitations, including a small sample size, and because of the single-center non-randomized design, the study findings could not be generalized.

Conclusion

The frequency of hypoglycemia was higher among middle-aged insulin-treated people with poor dietary compliance and poor diabetic education. The number of subjects taking conventional insulin therapy before the development of hypoglycemia was more than those who were taking oral hype hypoglycemic drugs. Improper dietary compliance appeared as a significant factor in hypoglycemia. Subjects who took reduced meals or omitted meals despite having antidiabetic drugs suffered more from hypoglycemic episodes. Again, subjects who did not follow dietary advice and did not adjust meals during illness and exercise experienced more hypoglycemia. The level of knowledge and practice in our diabetic population regarding home monitoring of blood glucose, early recognition of symptoms and signs, and prevention and treatment of hyperglycemia is not satisfactory. Hence, proper diabetic education about diet drugs, exercise techniques, use of insulin devices, and treatment of an associated systemic illness are the main factors for reducing hypoglycemic episodes in the diabetic population.

Conflict of interest: None declared

References

1. Cryer P. Hypoglycaemia: the limiting factor in the glycaemic management of type I and type II diabetes. Diabetologia. 2002;45(7):937–48.

2. International Hypoglycaemia Study Group. Hypoglycaemia, cardiovascular disease, and mortality in diabetes: epidemiology, pathogenesis, and management. lancet Diabetes Endocrinol. 2019 May;7(5):385–96.

3. Cryer PE, Davis SN, Shamoon H. Hypoglycemia in diabetes. Diabetes Care. 2003;26(6):1902–12.

4. Balijepalli C, Druyts E, Siliman G, Joffres M, Thorlund K, Mills EJ. Hypoglycemia: a review of definitions used in clinical trials evaluating antihyperglycemic drugs for diabetes. Clin Epidemiol. 2017;9:291.

5. Braithwaite SS, Buie MM, Thompson CL, Baldwin DF, Oertel MD, Robertson BA, et al. Hospital hypoglycemia: not only treatment but also prevention. Endocr Pract. 2004;10:89–99.

6. Group DC and CTR. Effect of intensive diabetes treatment on the development and progression of long-term complications in adolescents with insulin-dependent diabetes mellitus: Diabetes Control and Complications Trial. Diabetes Control and Complications Trial Research Group. J pediatr. 1994;125:177–88.

7. Frier BM. Morbidity of hypoglycemia in type 1 diabetes. Diabetes Res Clin Pract. 2004;65:S47–52.

8. Kagansky N, Levy S, Rimon E, Cojocaru L, Fridman A, Ozer Z, et al. hypoglycemia as a predictor of mortality in hospitalized elderly patients. Arch Intern Med. 2003;163(15):1825–9.

9. Standards of medical care in diabetes--2011. Vol. 34 Suppl 1, Diabetes care. 2011. S11-61 p.

10. Nordwall M, Arnqvist HJ, Bojestig M, Ludvigsson J. Good glycemic control remains crucial in prevention of late diabetic complications–the Linköping Diabetes Complications Study. Pediatr Diabetes. 2009;10(3):168–76.

11. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, et al. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2009 Jan;32(1):193–203.

12. Franciosi M, Pellegrini F, De Berardis G, Belfiglio M, Cavaliere D, Di Nardo B, et al. The impact of blood glucose self-monitoring on metabolic control and quality of life in type 2 diabetic patients: an urgent need for better educational strategies. Diabetes Care. 2001;24(11):1870–7.

13. Group UKPDS (UKPDS). Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998;352(9131):837–53.

14. Fischer KF, Lees JA, Newman JH. Hypoglycemia in hospitalized patients. Causes and outcomes. N Engl J Med. 1986 Nov;315(20):1245–50.

All correspondence to
Dr. Mohammad Motiur Rahman
Junior Consultant, Medicine,
Upazilla Health Complex, Puthia, Rajshahi
Email: anik.doc@gmail.com