Hypoglycemia in Type 2 Diabetes Mellitus: A Comparative Cross-Sectional Study in a Tertiary Care Hospital in Eastern Nepal

Uttar Kumar Mainali[1], Deepak Sigdel[2], Richa Sharma[3], Sarbesh Kumar Jha[4], Ragin Kathet[5], Manish Dahal[6], Praveen Kumar[7], Atul Dwivedi[8]

ABSTRACT

Introduction: Hypoglycemia is one of the most common complications of Diabetes Mellitus management. The reason could be an over enthusiastic approach in maintaining tight blood sugar control to reduce the long-term complications. s This study aimed to find out the prevalence of hypoglycemic events in Type 2 diabetics in a tertiary care hospital of Eastern Nepal alongwith awareness on hypoglycemia symptoms and knowledge on immediate measures to be taken during episode of hypoglycemia.

Material and methods: This comparative cross-sectional study was done in a tertiary care hospital in Eastern Nepal from 1st June 2018 to 31st October 2019. Ethical clearance was taken. Consecutive sampling was done during study period after taking informed verbal consent from patients. Various factors of hypoglycemia were noted and compared using SPSS-16 software.

Results: Out of 470 participants, 282 (60%) were male and 188 (40%) were female. The mean age of the participants was 51.96±11.37 years. Among them, 45.1 percent had hypoglycemic events prior to presentation with severe hypoglycemia in 6.8 percent. Similarly, 54.7 percent were aware of symptoms of hypoglycemia and only 27.9 percent had knowledge of immediate management of hypoglycemia. While travelling, only 4.7 percent used to carry sweets for immediate management of hypoglycemic symptoms. Significantly higher proportion of hypoglycemia was observed in those with longer duration of diabetes i.e. ≥ 10 years, in those using insulin and in female patients.

Conclusion: Hypoglycemia is quite prevalent amongst people with type 2 diabetes on treatment particularly those on insulin. Hence, Physicians and diabetes educators have to play an important role in educating diabetes patients while treating them on hypoglycemia so that hypoglycemia related morbidity and mortality can be reduced or prevented.

Keywords: Hypoglycemia; Diabetes Mellitus, Type 2; Awareness

INTRODUCTION

Diabetes mellitus (DM) is well recognized as a global healthcare burden of 21st century. The number of patients of DM has been continuously increasing over the past few decades. As a matter of fact, the huge number of adult diabetic patients in India has earned it the dubious title of being termed as the diabetes capital of the world. Even after the availability of numerous effective antidiabetic drugs and regimes, the management of diabetes is often complicated by certain barriers. One of the most important of these barriers is hypoglycemia.[1-3]

A close look at the blood sugar and HbA1c levels reveals that despite medication, the patient's blood sugar levels remained significantly high. It is not entirely new finding though surprising to us. The slight improvement in glycemic control may be attributed to the patient's recruitment to the study when they become more compliant to treatment as well as become more conscious of their diet.[4,5] Hypoglycemia can lead to coma and even death, depending on its severity or duration.[2] There can be a six fold higher incidence of death, increased costs of medical care, and loss of productivity due to hypoglycemia. The American Diabetes Association defines the hypoglycemia as "any abnormally low plasma glucose concentration that exposes the subject to potential harm" and proposes a threshold of <70 mg%.[6] Although many studies have been conducted on awareness of hypoglycemia, very few studies have mentioned on other aspects of hypoglycemia including knowledge of symptoms, precipitating factors, prevention, and immediate action to be taken during an episode of hypoglycemia. In Nepal, there are only few studies on the prevalence of hypoglycemia awareness and its relationship with hypoglycemic events. We didn't find any study conducted in Nepalese diabetic patients on prevalence of hypoglycemia till date of start of this study. This study aimed to find out the prevalence of hypoglycemic events in Type 2 diabetics

[1]Endocrinologist, Department of Medicine, Koshi Hospital, Biratnagar, Nepal, [2]Head of Department, Department of Medicine, Koshi Hospital, Biratnagar, Nepal, [3]Dermatologist, Department of Dermatology, Koshi Hospital, Biratnagar, Nepal, [4]Cardiologist, Department of Medicine, Koshi Hospital, Biratnagar, Nepal, [5]Radiooncologist, Department of Oncology, Koshi Hospital, Biratnagar, Nepal, [6]Physician (Internist), Department of Medicine, Koshi Hospital, Biratnagar, Nepal, [7]Pediatrician, Department of Pediatrics, Koshi Hospital, Biratnagar, Nepal, [8]Ex- Research fellow, Zhengzhou University, Ex- Associate Professor-Department of Clinical and Basic Sciences, Medial College of Hubei Polytechnic University, Hubei, Huangshi, P R China

Corresponding author: Dr Uttar Kumar Mainali, Koshi Hospital, Biratnagar, Nepal, Postal code - 56613

MATERIAL AND METHODS

A comparative cross-sectional study was carried out in the endocrine clinic of Koshi Hospital, Biratnagar from 1st June 2018 to 31st October 2019 after taking ethical clearance from Institutional Ethical Committee of Koshi Hospital. This study was conducted on type 2 Diabetes Mellitus patients who had visited the endocrine clinic during study period. They had voluntarily and verbally consented for participation. Clinically diagnosed cases of diabetes other than Type 2 Diabetes like Type 1 Diabetes, MODY (Maturity Onset Diabetes of Young) and LADA (Latent Autoimmune Diabetes in Adults) were excluded from the study. Data collection instrument was developed by the researchers around the objectives of the study and to suit the Nepali environment through robust review of literature on previous studies on hypoglycemia. Expert comments were obtained by the experts who were involved in diabetic treatment and research. The questionnaire comprised socio-demographic variables, duration of diabetes, symptoms of hypoglycemia, knowledge on immediate measures to be taken for relief of hypoglycemic symptoms and type of anti-diabetic medications. Consecutive sampling method was used to enroll participants from 1st June 2018 to 31st Oct 2019.

Sample size was calculated using the formula

$n = Z^2 \times p \times (1-p)/e^2$

Where,

n = sample size

p= 45%; prevalence of hypoglycemia among diabetes patients on the basis of review article by Chloe L. Edridge et al.[10]

e = margin of error (10%) = 4.5

Z= 1.96 at 95% Confidence interval.

The calculated sample size was 470. Operationally, adult patients were classified based on their age into young adults who were aged less than 60 years and elderly patients who were aged 60 years and more. The data were analyzed by using SPSS version 16 software. Categorical variables were described by frequencies and percentages. Point estimate at 95% Confidence Interval was calculated along with frequency and proportion for binary data. Chi-square test was used to test any significant association between categorical variables. In all cases, P < 0.05 was considered statistically significant.

RESULTS

Out of 470 patients, 212 (45.1%) had hypoglycemic events prior to presentation to clinic; 61 (13%) had one episode while rest 151 (32.1%) had more than one episode till date of presentation to clinic. A total of 32 (6.8%) of patients had a history of hospitalization due to hypoglycemia in the past. Regarding hypoglycemia awareness, 257(54.7%) of them were aware of symptoms of hypoglycemia and only 131 (27.9%) had knowledge of immediate management of hypoglycemia **(Table 1).** While travelling, only 22 (4.7%) of total patients would carry sweets with them. Similarly, not a single patient would carry any identity card mentioning their illness of diabetes mellitus while travelling.

In our study, 282 (60%) were male and 188 (40%) were female. Mean age of participants was 51.96±11.37 years. Of them, 130 (27.7%) were elderly patients (≥60 years). Similarly, 391 (83.2%) had received some form of formal education in life and 459 (97.7%) had some family members living with them who could care about their illness even in emergency conditions taking them into hospital if necessary. Of them, 268 (57%) had diabetes of less than 5 years duration, 88 (18.7%) had that of 5 to 10 years and rest 114 (24.3%) had of ≥10 years. HbA1C was good (< 7%) in 69 (14.7%) patients; ≥7 to < 10% in 183 (38.9%) patients; and poorly controlled (≥ 10%) in 98 (20.9%) patients. Similarly, 256 (54.5%) had some first degree relatives suffering from diabetes. Understanding of disease itself was good in 218 (46.4%) while only fair in 174 (37%) and rest 78 (16.6%) had poor understanding of the disease. Regarding comorbidities, 187 (39.8%) had hypertension, 24 (5.1%) had heart disease and 18 (3.8%) had chronic kidney disease.

Only 11 (2.3%) had their meal habit as per dietitian's advice; 43 (9.1) percent were having low carb low fat diet without calculation as per health workers' advice and rest 416 (88.5%) were having normal diet like other family members. Similarly, 209 (44.5) percent of them had a habit of exercise as per health worker's recommendation while 128 (27.2) percent would exercise only on an occasional basis and rest 133 (28.3) percent were not following physical activities required. Out of the total study population, 54 (11.5) percent were on insulin at home; 23 (4.9) percent were using premixed human insulin and rest 34 (6.6%) were on some form of analogue insulin either premixed or basal. Regarding self monitoring of blood glucose at home (SMBG), 23 (4.9%) percent patients used glucometer at home to check blood glucose level ≥1 time per week, 269 (7.2%) monitored ≥1 time per month while 92 (19.6%) monitored occasionally and rest 86 (18.3%) never monitored blood glucose at home.

Variable		n (%)
Hypoglycemia	Once since start of treatment	61 (13.0)
	≥1 times	151 (32.1)
Number of patients with Hypoglycemia requiring hospitalization		32 (6.8)
Awareness of hypoglycemic symptoms		257 (54.7)
Knowledge on immediate management of hypoglycemia		131 (27.9)
Table-1: Proportion of hypoglycemia and hypoglycemia awareness.		

Background characteristic	n (%)
Age	
≥60 years	130 (27.7)
<60 years	340 (72.3)
Sex	
Male	282 (60.0)
Female	188 (40.0)
Education	
Literate	391 (83.2)
Illiterate	79 (16.8)
Duration of Diabetes in years	
≥10 years	114 (24.3)
<10 years	356 (75.7)
Insulin use	
Yes	54 (11.5)
No	416 (88.5)
Comorbidities	
Hypertension	187 (39.8)
Heart disease (IHD/CHF)	24 (5.1)
Chronic kidney disease	18 (3.8)
Complications of Diabetes	
Retinopathy	77 (16.38)
Peripheral neuropathy	127 (27.02)
Sexual problems	19 (4.0)
IHD: Ischemic heart disease CHF: Congestive Heart Failure	

Table-2: Background characteristics of Type 2 Diabetes Mellitus patients

Regarding complications, 239 (50.9%) were aware of macro and microvascular complications. Out of total patients, diabetes related ophthalmological complications were found in 77 (16.4%), neuropathy related problems in 127 (27%), sexual problems in 19 (4%) and dental problems in 25 (5.3%) patients (Table 2).

Those having history of hypoglycemia were compared with those not having history of hypoglycemia with respect to various characteristics as illustrated in Table 3.

DISCUSSION

Hypoglycemia is the rate limiting complication in the achievement of strict glycemic control in diabetes management. Significant episodes of hypoglycemia and its attendant counter-regulatory hormonal response lead to poor glycemic control. The former may also be associated with cardiovascular and cerebrovascular morbidities. Large trials (action to control cardiovascular risk in diabetes, Veterans affairs diabetes trial) have shown that there were was a higher mortality in the group that had hypoglycemia (intensively treated arm.[5-7] This study identified prevalence of hypoglycemia in 470 ambulatory type 2 Diabetes Mellitus patients. In addition, awareness of hypoglycemic symptoms and knowledge on immediate measures to be taken for relief of hypoglycemic symptoms were also assessed. We didn't

Background characteristic	Hypoglycemia (%)	No hypoglycemia (%)	p value
Age			
≥ 60 years	42.4	57.6	.073
< 60 years	51.5	48.5	
Sex			
Male	41.1	58.9	**.045**
Female	50.5	49.5	
Education			
Literate	44.2	55.8	.530
Illiterate	48.1	51.9	
Duration of Diabetes in years			
≥ 10 years	65.8	34.2	**< .001**
< 10 years	38.2	61.8	
Insulin use			
Yes	85.2	14.8	**< .001**
No	39.8	60.2	
COMORBIDITIES			
Hypertension			
Yes	50.3	49.7	.057
No	41.3	58.7	
Heart disease (IHD/CCF)			
Yes	66.7	33.3	**.028**
No	43.7	56.3	
Chronic Kidney Disease			
Yes	44.4	55.6	.969
No	45	55	
COMPLICATIONS			
Retinopathy			
Yes	59.7	40.3	**.004**
No	42	58	
Peripheral neuropathy			
Yes	51.2	48.8	.095
No	42.6	57.4	
IHD: Ischemic heart disease CHF: Congestive Heart Failure			

Table-3: Proportion of hypoglycemia by background characteristics in Type 2 Diabetes mellitus patients

find any study conducted in Nepalese diabetes patients on prevalence of hypoglycemia till date.

In our study 45.1% of total patients reported symptoms suggestive of hypoglycemia like dizziness, palpitation, sweating, altered sensorium since diagnosis of their disease which was comparable to prevalence of 45% reported in a systematic review of literature on the prevalence of hypoglycemia by Edridge et al.[7] But this proportion of hypoglycemia found in our study was less than the prevalence shown by studies on similar population in other parts of developing world; India - 96%,[8] Brazil-61.8%,[9] and more than that found in a Nigerian study.[10] Similarly we found 7.1 percent prevalence of severe hypoglycemia in our study population which was defined as need of assistance of others or those events requiring hospitalization for the management of symptoms suggestive of hypoglycemia like severe weakness and altered sensorium. This prevalence was lower than that found in a Tukish study by Buyukkaya Bessen et al,[11] which showed severe hypoglycemic events in the 15.5% of study population. The variable prevalence of hypoglycemic events in this study and the referenced studies could be attributed to epidemiological characteristics of the study population such as demographic and ethnic variations, methods of reporting and wide spectrum of therapeutic regimens used in the management of diabetes mellitus.

Regarding hypoglycemia awareness, a similar study conducted in Karnatak, India by Pai SA and George [12] showed average awareness in 54% of participants which is almost similar to our finding of 54.7%. The same study from Karnatak India showed that 49% consumed glucose powder or sugar with water as an immediate measure but only 27.9% in our study had such type of knowledge on immediate management of hypoglycemia. This difference could be due to demographic variations of study population including literacy status. Moreover, only 4.7% of total patients in our study would make sure to carry sweets with them and none of them had any identity card mentioning their illness while travelling. This poor scenario of awareness during travel has to be considered seriously especially while managing our patients in diabetes clinics. The immediate treatment of hypoglycemia should be known by all the diabetic patients, so that the need for hospitalization and possible fatal consequences could be avoided. Illiterate patients and elderly patients with dementia or without other family members to care must be more educated about hypoglycemia. Thus, improving patient skills on self-management, self-monitoring of sugar and adjustments of dose based on requirements can reduce the risk of hypoglycemia.

In this study, no significant difference in proportion of hypoglycemia was found with respect to age, literacy status, meal habit and HbA1C level. However, a significantly higher proportion of hypoglycemia was observed in those with longer duration of diabetes i.e. ≥ 10 years (p value < 0.001), in those using insulin (p < 0.001) and in female patients (p = 0.045). Higher frequencies of hypoglycemia in those with insulin use has been shown by many studies in the past including interventional study UKPDS trial[13] and observational study conducted in Karnataka, India.[12] Samya V et al assessed the prevalence of Hypoglycemia among Patients with Type 2 Diabetes Mellitus in a Rural Health Center. 390 patients with type 2 diabetes mellitus getting treated in a primary health center were assessed for symptoms of hypoglycemia. Prevalence of hypoglycemia was 57.44%. Severe hypoglycemia was found in 10.7% of the patients. The first reported symptom of hypoglycemia was dizziness (72.3%). The most common etiological factor leading to hypoglycemia was missing a meal (89.3%). Females were at a significant higher risk of developing hypoglycemia. Their study has established the high prevalence of self-reported hypoglycaemia in the rural settings where resources are limited to monitor the glucose levels.[14]

Recurrent episodes of hypoglycemia result in hypoglycemia unawareness. Hypoglycemic episodes, especially if severe or recurrent may result in significant psychosocial dysfunction and lower quality of life. In spite of the knowledge about the importance of hypoglycemia, it is still a relatively neglected complication in diabetes care in our setting.[15-19] In a survey conducted among 2530 Americans with type 2 diabetes, 55% reported having experienced hypoglycemia in the past. The India Hypoglycemia Study Group highlights that there is negligible data on the epidemiology of hypoglycemia in type 2 diabetes from India, which has the second largest number of diabetes patients in the world.[20-23] A retrospective review of 102 patients (90% with Type 2 diabetes) admitted to hospital with drug-induced hypoglycaemic coma revealed a mortality rate of 4.9% (n = 5) (all in patients with Type 2 diabetes). However, it was not possible to confirm whether the deaths were due to hypoglycaemia, since all five patients had serious comorbidities. Coma was associated with considerable morbidity, including head trauma, fracture, seizures, transient asymptomatic myocardial ischaemia and stroke.[23,24]

CONCLUSION

This study shows that hypoglycemia is quite prevalent amongst people with type 2 diabetes on treatment, particularly those on insulin. Though awareness of hypoglycemia symptoms and its early management was average among diabetics, very few proportions of diabetics carried any source of simple sugars. Initiation of home care or on the spot care while travelling by taking simple sugars like glucose, sugar or chocolates followed by hospitalized care if necessary is the most ideal way to prevent severe spells of hypoglycemia. Hence, the primary care physicians and diabetes educators have to play an important role in educating diabetics on hypoglycemia stressing on symptoms and immediate measures to be taken so that hypoglycemia related morbidity and mortality can be reduced or prevented.

ACKNOWLEDGMENT

this study would have been incomplete.

REFERENCES

1. Leiter LA, Yale JF, Chiasson JL, Harris SB, Kleinstiver P, Sauriol L. Assessment of the impact of fear of hypoglycemic episodes on glycemic and hypoglycemia management. Can J Diabetes. 2005;29:186–92.
2. Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP, Jr, Selby JV. Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. JAMA. 2009;301:1565–72.
3. Frier BM, Schernthaner G, Heller SR. Hypoglycemia and cardiovascular risks. Diabetes Care. 2011;34:S132–7.
4. Bhutani G, Kalra S, Lamba S, Verma PK, Saini R, Grewal M. Effect of diabetic education on the knowledge, attitude and practices of diabetic patients towards prevention of hypoglycemia. Indian J Endocrinol Metab. 2015;19:383.
5. Akkineni S, Mathews AM, Apuroopa G, Sridhar NN, RODRIGUES PA. A study on patients awareness, recognition management and prevalence of hypoglycemic episodes in type 2 diabetes mellitus in a tertiary care hospital. Asian J Pharm Clin Res. 2015;8:390–394.
6. Association AD. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2019. Diabetes Care. 2019;42:S61.
7. Edridge CL, Dunkley AJ, Bodicoat DH, Rose TC, Gray LJ, Davies MJ, et al. Prevalence and incidence of hypoglycaemia in 532,542 people with type 2 diabetes on oral therapies and insulin: a systematic review and meta-analysis of population based studies. PloS One. 2015;10(6).
8. Shriraam V, Mahadevan S, Anitharani M, Jagadeesh NS, Kurup SB, Vidya TA, et al. Reported hypoglycemia in Type 2 diabetes mellitus patients: Prevalence and practices-a hospital-based study. Indian J Endocrinol Metab. 2017;21:148.
9. Lamounier RN, Geloneze B, Leite SO, Montenegro R, Zajdenverg L, Fernandes M, et al. Hypoglycemia incidence and awareness among insulin-treated patients with diabetes: the HAT study in Brazil. Diabetol Metab Syndr. 2018;10:1–10.
10. Iloh GUP, Amadi AN. Epidemiology of hypoglycemia among ambulatory Type 2 diabetic patients in a primary care clinic of a tertiary hospital in Southeastern Nigeria. J Health Res Rev. 2018;5:57.
11. Besen DB, Sürücü HA, Koşar C. Self-reported frequency, severity of, and awareness of hypoglycemia in type 2 diabetes patients in Turkey. PeerJ. 2016;4:e2700.
12. Pai S, George P. Study on Awareness of Symptoms of Hypoglycaemia & Early Management among Patients with Diabetes. J Dent Med Sci. 2015;14:11–13.
13. Group UPDS (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). The lancet. 1998;352:837–853.
14. Samya V, Shriraam V, Jasmine A, et al. Prevalence of Hypoglycemia Among Patients With Type 2 Diabetes Mellitus in a Rural Health Center in South India. J Prim Care Community Health. 2019;10:2150132719880638.
15. Vignesh JP, Mohan V. Hypoglycaemia unawareness. J Assoc Physicians India 2004;52:727-32.
16. Ziemer DCGoldschmid MMusey VC et al. Diabetes in urban African-Americans, III: management of type II diabetes in a municipal hospital setting. Am J Med. 1996;10125- 33
17. Schwartz NSClutter WEShah SDCryer PE Glycemic thresholds for activation of glucose counterregulatory systems are higher than the threshold for symptoms. J Clin Invest. 1987;79777- 781
18. Mitrakou ARyan CVeneman T et al. Hierarchy of glycemic thresholds for counterregulatory hormone secretion, symptoms and cerebral dysfunction. Am J Physiol. 1991;260E67- E74
19. Fanelli CPampanelli SEpifano L et al. Relative roles of insulin and hypoglycaemia on induction of neuroendocrine responses to, symptoms of, and deterioration of cognitive function in hypoglycaemia in male and female humans. Diabetologia. 1994;37797- 807
20. Kalra S, Mukherjee JJ, Venkataraman S, Bantwal G, Shaikh S, Saboo B, et al. Hypoglycemia: The neglected complication. Indian J Endocrinol Metab 2013;17:819-34.
21. Survey Reveals Low Hypoglycemia Awareness among Patients with Diabetes. Endocrine Today, May 2011. American Association of Clinical Endocrinologists 20th Annual Meeting. Available from: http://www.healio.com/endocrinology/diabetes/news/print/endocrine-today/%7Be3d5b9ab-65d9-4796-890b-3b69df497be4%7D/survey-reveals-low-hypoglycemia-awareness-among-patients-with-diabetes. [Last accessed on 2014 Aug 22].
22. Viswanathan M, Joshi SR, Bhansali A. Hypoglycemia in type 2 diabetes: Standpoint of an experts' committee (India hypoglycemia study group). Indian J Endocrinol Metab 2012;16:894-8.
23. Ben-Ami H, Nagachandran P, Mendelson A, Edoute Y. Drug-induced hypoglycemic coma in 102 diabetic patients. Arch Intern Med. 1999;159:281–284.
24. Nattrass M, Lauritzen T. Review of prandial glucose regulation with repaglinide: a solution to the problem of hypoglycemia in the treatment of type 2 diabetes? Int J Obesity. 2000;24:S21–S31.