

Frequency of Hypoglycemia in Insulin-Treated Patients of Type 2 Diabetes Mellitus

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ABSTRACT

Objective: Our study was designed to explore the frequency of hypoglycemia events in type 2 diabetic patients. We further aimed to correlate the hypoglycemia events with treatment regimes and diabetes duration.

Place and Duration: Mayo Hospital Endocrine Outpatient Department. From 1-04-2022 to 30-06-2022.

Study type: Clinical based study

Methodology: We used the already tested questionnaire from the American Diabetes Association and The Endocrine Society to collect the relevant information. The questionnaire was translated into the local language to facilitate the interview. Copies of the questionnaire were distributed to 1000 patients at the study site. The questionnaire was based on socio-demographic and clinical information including gender, age, duration of diabetes, treatment, frequency of hypoglycemia events, and symptoms. Chi-square was used to analyze the association of risk factors. While odd ratios were also computed at a 95% confidence interval. P-value <0.05 was considered for statistical significance.

Results: Total of 360 cases T2DM had hypoglycemic events with a prevalence of 36%. The mean age of patients was reported as 51 years. A total of 200 cases were found in the mentioned age group with a 55.56% prevalence. Elderly age patients were also the secondary target of hypoglycemia with a prevalence ratio of 27.78%. Out of these 360 patients, 320 (86.11%) had mild to moderate hypoglycemia with symptoms of eye tarnishing, tremors, numbness of the tongue, and drowsiness while 15% of cases lost their consciousness and were categorized as severe events of hypoglycemia.

Conclusion: The study concluded on a note that insulin-treated patients should be aware of the hypoglycemia events because in these cases the risk is comparatively high than in others.

Keywords: Diabetes mellitus, Insulin, Hypoglycemia

INTRODUCTION

Diabetes Mellitus is one of the major worldwide burden on health department. The frequency of type 2 diabetes has been increasing in poor countries.¹ Initially, diabetes was developed in urban areas due to poor lifestyles however many cases had been found in rural and urban areas of developing countries.² The ten-year survey reported more prevalence of diabetes in villages than the cities.³ Despite the availability of treatment acquiring glycemic targets remains a great challenge. Comprehensive disease management strategies and therapies help in achieving glycemic goals and slowing down the T2DM progression.^{4,5} Numerous diabetic control departments indicated that during the treatment of T2DM maintaining tight glycemic control is very important so that the chances of complications could be minimized.^{6,7} However, aggressive diabetic therapy enhanced the risk of hypoglycemia events. Three randomized clinical trials revealed a three-fold increase risk of hypoglycemic episodes while managing glycemic goals.^{8,9,10} These episodes enhance the risk of cardiovascular complications resulting in patient death.¹⁰ American diabetes association suggested the guidelines of plasma glucose maintenance should not be strictly followed especially in treating the elderly population with co-morbidities to reduce the risk of developing hypoglycemia.¹¹ While European Association for the Study of Diabetes (EASD) guidelines suggested that the risk of hypoglycemia should be considered while treating the patients.¹² Insulin and sulfonylureas drug is the primary cause of hypoglycemic events in 90% of diabetic patients.¹³⁻¹⁶

Hypoglycemia is a condition in which patients observed episodes of low plasma concentrations which put their life at threat.¹⁷ Usually, a plasma level less than 70 mg/dL (3.9 mmol/L) is recognized as a condition of hypoglycemia however it may happen with symptoms or without symptoms.¹⁸ Hypoglycemia can be managed by repressing the endogenous insulin secretion and glycogen stimulation. These all procedures assist in cutting down the glucose utilization in peripheral tissues and raising plasma glucose levels.¹⁹ Whipple's triad is a standard technique to evaluate the symptoms associated with hypoglycemia which

provides a better understanding of symptoms relief and elevation of plasma glucose levels.²⁰ With the help of this method, physicians can be easily diagnosed patients with hypoglycemia. Pathophysiology of hypoglycemia centered around the beta cell failure which leads to the failure of alpha cells which affects the glucose regulation.²¹ The progression and incidence rate of hypoglycemia is comparatively less in type 1 diabetes however type 2 diabetic patients had more events of hypoglycemia with high intensity. Growing incidents of diabetes and modalities of intense blood glucose management increase the risk of hypoglycemia incidents.²²

With these previous remarks, our study was designed to explore the frequency of hypoglycemia events in type 2 diabetic patients. We further aimed to correlate the hypoglycemia events with treatment regimes and diabetes duration.

METHODOLOGY

For this study convenience sampling was used to gather the data of T2DM patients from the outpatient department of hospital from September ... to June..... This study used the already tested questionnaire from the American Diabetes Association and The Endocrine Society²³ to collect the relevant information. The questionnaire was translated into the local language to facilitate the interview. Copies of the questionnaire were distributed to 1000 patients at the study site. The questionnaire was based on socio-demographic and clinical information including gender, age, duration of diabetes, treatment, frequency of hypoglycemia events, and symptoms. Patients with type 1 diabetes, gestational diabetes, and newly diagnosed patients were excluded. Whipple triad criteria were used to analyze the symptoms caused by hypoglycemia especially, low-level plasma glucose at the time of symptoms, and symptoms relief when glucose levels become normal. Patients were asked about their previous experiences of hypoglycemia in the past 2 to 3 months. If they experienced 2 to 3 times in a month and symptoms relief after consuming food, juices, or sugar then it was considered a hypoglycemia episode.²⁴ The self-checked plasma glucose with a glucometer, clinical history, and

symptomatic relief was considered for the estimation of the prevalence of hypoglycemia. The hypoglycemia event which required medical assistance were documented as severe episodes of hypoglycemia. Each patient was interviewed for 30 minutes. Complete clinical examination was done for each patient along with blood samples to evaluate the HbA1c levels.

Statistical Analysis: Data analysis was performed by using SPSS version 24.0. Frequency and percentages were used to analyze the variables. Chi-square was used to analyze the association of risk factors. While odd ratios were also computed at a 95% confidence interval. P-value <0.05 was considered for statistical significance.

RESULTS

In this study total of 1000 T2DM cases were reported. Out of these 360 had hypoglycemia events with a prevalence of 36%. The mean age of patients was reported as 51 years. Among these individuals, 58% were female while 42% were male. The results revealed that patients in the age groups ranging from 40- 60 years were more vulnerable to hypoglycemia. A total of 200 cases were found in the mentioned age group with a 55.56% prevalence. Elderly age patients were also the secondary target of hypoglycemia with a prevalence ratio of 27.78%. Out of these 360 patients, 320 (86.11%) had mild to moderate hypoglycemia with

symptoms of eye tarnishing, tremors, numbness of the tongue, and drowsiness while 15% of cases lost their consciousness and were categorized as severe events of hypoglycemia. A total of 259 (71.9%) patients were on insulin treatment of which 6 cases had T2DM in less than one year, 54 cases had a 5-year history of T2DM, and 199 cases reported diabetes for more than 5 years. A significant correlation was found between diabetes duration and hypoglycemia events (p <0.001). In the current study, a statistically significant association was found between hypoglycemia events and co-morbidities in T2DM cases (p <0.001) However, no significant difference was found between the cases who consume snacks after meals and who did not (p=0.282).

Table 1: Socio-demographic and clinical characteristics of patients²⁵

Variables	Total cases N (%)
Hypoglycemia cases	360 (36%)
<40 Years	60 (16.67%)
41-60 Years	200 (55.56%)
>60 Years	100 (27.78%)
Mild to moderate	320 (86.11%)
Severe	55 (15.28%)
No occurrence of hypoglycemia	640 (64%)

Table 2: Comparison between treatment modalities, diabetes duration and hypoglycemia²⁵

Variables	Diabetes duration	Hypoglycemia attacks	Chi-square		Odd ratios	95% CI	P-value
			X ²	P-value			
Insulin	Less than one year	6 (2.32%)	19.846	<0.001	2.952	2.237-3.895	<0.001
	1-5 years	54 (20.85 %)					
	More than 5 years	199 (76.83 %)					
Oral tablets	Less than one year	9 (9.47%)	4.476	0.034	0.343	0.259-0.455	<0.001
	1-5 years	40 (42.11%)					
	More than 5 years	46 (48.42%)					
Both	1-5 years	0 (0%)	1.976	0.160	0.706	0.272-1.837	0.476
	More than 5 years	6 (100%)					

Table 3: Comparison between other diseases, snack intake and hypoglycemia²⁵

Variables	Hypoglycemic attacks	Chi-square	P-value
Co-morbidities		32.176	<0.001
Yes	227 (63.06%)		
No	133 (36.94%)		
Snacks		1.157	0.282
Yes	152 (42.22 %)		
No	208 (57.78%)		

DISCUSSION

Hypoglycemia in diabetic patients is a threatening condition that especially occurs in those cases who used treatment to increase insulin levels. The current study focused on the frequency of hypoglycemia events about treatment modalities and duration of events. All the patients aged 18-80 years with an average age of 51 years were recruited. Out of 1000 patients, a total of 360 patients reported hypoglycemia events. Prevalence of hypoglycemia was reported as 36%. These results are comparatively less than the previous studies of Samya et al²⁴, Marrett et al²⁶ and Shriram et al²⁷. Study Samya et al found that 224 cases of type 2 diabetes had hypoglycemia. The total prevalence of hypoglycemia was reported as 57.43% in their study. Meanwhile, a study by Marrett et al reported a 63% prevalence and Shriram had 78.1% which fit in the definition of hypoglycemia symptom on intake of glucose.

In the current study, 86.11% of cases of hypoglycemia were mild to moderate while only 15.28% reported severe events similar to the Henderson et al.²⁰ A retrospective study by Henderson et al reported an annual 15% prevalence of hypoglycemia in type 2 diabetic patients. A study by Gehlout et al²⁸ revealed 21% cases of severe, 51% mild, and 28.3% cases of hypoglycemia. Meanwhile,

these results are comparatively high than the previous study by Marrett et al²⁶ and Samya et al²⁴ in which they reported 13% and 10% severe cases respectively. A study conducted by the American Association of Clinical Endocrinologists²⁹ revealed that 20% of cases required medical assistance for hypoglycemic episodes while 6% required hospitalization. In their survey severity of the disease is much higher than ours.

In the current study, 48.42% of patients had type 2 diabetes for more than 5 years. A total of 76.83% of patients on insulin reported hypoglycemia attacks. The results showed a positive correlation between the insulin-treated hypoglycemia cases and the duration of diabetes. These results are consistent with the previous study conducted on the United Kingdom population in which they revealed that patients with more than 15 years of diabetic history had more incidents of hypoglycemia. A retrospective study by Miller et al³⁰, reported 16% hypoglycemia among T2DM patients on oral hypoglycemic agents while 30% prevalence was reported in those treated with insulin.

Regarding self-awareness of hypoglycemia current study found that 23.61% of cases always predict hypoglycemia, 22.22% usually reported while 26.36% sometimes predict hypoglycemia and 27.72% had no awareness. Comparing these results with international literature we found that the study of Pedersen-Bjergaard observed a 49.94% ratio of impaired awareness of hypoglycemia and a 27.72% ratio of unawareness. Meanwhile, in Turkey, 83.4% of type 2 diabetic patients had impaired awareness of their hypoglycemia.³¹ The accuracy of self-reported hypoglycemia prevalence may have been affected by patient recall especially in mild cases.

The missed meal is a major reason for hypoglycemic events. The American Association of Clinical Endocrinologists²⁹ found missed meals as an etiological factor in 87% of cases of T2DM. In

the current study, a statistically significant association was found between hypoglycemia events and co-morbidities in T2DM cases. However, no significant difference was found between the cases who consume snacks after meals and who did not.

CONCLUSION

The study concluded on a note that insulin-treated patients should be aware of the hypoglycemia events because in these cases the risk is comparatively high than in others. Patients with other diseases are also at high risk and required proper management strategies.

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