 doi:10.20944/preprints202209.0153.v3

*Article*

# Risk of hospitalization in diabetic patients with severe hypoglycemia: a single-center study

**Leonardo Pieramati [1,*], Enzo Mantovani [2], Giuseppe Lucchini [3] and Massimo Amato [1]**

[1] Emergency Department, ASST Carlo Poma, Mantua, Italy
[2] Diabetology and Metabolic Diseases, ASST Carlo Poma, Mantua, Italy
[3] Biostatistical Service, ASST Carlo Poma, Mantua, Italy
* Correspondence: leonardo.pieramati@asst-mantova.it

**Abstract:** Background: Severe hypoglycemia is defined as low blood glucose levels that requires another person to be treated. Severe hypoglycemia is an emergency and is a complication that can occur in people taking insulin and some anti-diabetic drugs. The aim of our study was to evaluate the risk factors associated with hospitalization. Methods: We performed a retrospective study based on the clinical records of adults with severe hypoglycemia who were admitted consecutively to the Emergency Department (ED) of the Carlo Poma Hospital from January 2021 to December 2021. Results: Overall, 50 patients were identified and most of these were elderly patients with multiple comorbidities. They were treated with oral hypoglycemic drugs such as sulfonylureas or glinides (42%), insulin (46%) or both (6%). Hospitalization rates and in-hospital deaths occurred in 62% and in 4%, respectively. No risk factors were statistically significant correlated with hospitalization. The frailty of the elderly patients and their comorbidities were often the reason of hospitalization, rather than the episode of severe hypoglycemia. Conclusions: In our study, episodes of severe hypoglycemia can be a sign of the frailty of elderly diabetic patients and poor home care, who often require hospitalization.

**Keywords:** hypoglycemia; hospitalization; diabetes

## 1. Introduction

Severe hypoglycemia is defined as low blood glucose concentrations that requires assistance by another person to be treated [1]. Severe hypoglycemia is the most common and feared complication by diabetic patients as it interferes with a wide range of daily activities with negative repercussions on physical and psychological well-being. In severe hypoglycemia, neuroglycopenia can cause seizures, coma, permanent neurological damage and death. Identifying a cut-off that defines hypoglycemia is not easy because the glycemic thresholds for the onset of symptoms are influenced by chronic exposure to low glycemic levels [2]. However, in order to prevent episodes of severe hypoglycemia, the clinicians give instructions to patient to recheck his blood sugar in a short time when the value is ≤ 3.8 mmol/L (70 mg/dL) [3]. Recently, it has been proposed that a value of 3 mmol/L (54 mg/dl) identifies clinically significant hypoglycemia, which should be reported in clinical trials on hypoglycemic drugs in order to capture hypoglycemic episodes of greater clinical significance [4].

Hypoglycemia increases the risk of cardiovascular events [5, 6], dementia [7, 8], fractures [9, 10] and mortality [11], reducing quality of life [12, 13] and generating fear of hypoglycemic treatment [14] and consequently constitutes a limit to the achievement of good glycemic control. So now the definition of an optimized glycemic control should also include a low risk of hypoglycemia. Episodes of severe hypoglycemia are associated with an increased consumption of resources, both for the intensification of blood glucose self-monitoring, and for access to the EDs and hospitalization [15, 16]. Severe hypoglycemia is the principal cause of hospitalization rather than acute hyperglycemic complications [17] and at the same time it represents the main cause of access to the EDs for adverse drug

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events, secondary only to cumarolic overdose [18]. In addition to the direct costs, hypoglycemia causes important indirect costs linked to the loss of productivity [19].

## 2. Materials and Methods

We performed a retrospective study identifying all cases of severe hypoglycemia among diabetic patients, who attended the ED of Carlo Poma Hospital over the period between January 2021 and December 2021. Type 2 diabetes was defined in accordance with the 2021 criteria of the American Diabetes Association (ADA) [20].

Initially, we searched patients with blood glucose levels less than 3.8 mmol/L (70 mg/dL) at ED admission from an electronic records, so identifying a total of 234 patients. We excluded patients without previously known diabetes (n = 163) and without complete data (n = 21) from statistical analysis. As a result of this selection, 50 patients (33 men and 17 women) were included in final analysis.

The local ethics committees approved the study protocol. The informed consent requirement for the study was exempted by the ethics committee, because researchers only accessed retrospectively a de-identified database for analysis purposes.

Information on age, sex, type of diabetes, blood glucose concentrations measured in ED, use of hypoglycemic drugs, emergency codes given at the triage, rates of hospital admission and in-hospital mortality were extracted by the ED's electronic databases. Information on the main comorbidities and the clinical symptoms was also recorded.

## 3. Statistical Analysis

Continuous variables were reported as mean (standard deviation), while categorical data are reported as numbers and percentage. Comparisons between groups were carried out with an independent t-test for continuous variables and chi-squared test for categorical variables. All statistical tests were two-sided, and associations were considered statistically significant when the values were below a nominal level of 0.05 ($p < 0.05$). Calculations were performed with IBM SPSS Statistics software version 27.

## 4. Results

50 patients were included in the study, 46 (92%) patients had type 2 diabetes, 3 (6%) had type 1 diabetes and the last patient had steroid diabetes. Overall, 33 (66%) were male and the mean age was 78 years (25 - 96). Blood glucose concentrations measured in the ED's laboratories were 2.25 ± 0.77 mmol/L (41 ± 14 mg/dL).

Table 1 show patient characteristics. Most patients had one or more comorbidities, such as hypertension (occurring in 78% of cases), ischemic heart disease (42%), atrial fibrillation (38%), chronic kidney disease (54%), previous ischemic stroke (26%) or respiratory disease (20%). SARS-CoV-2 infection was present in 1 patient (2%). We found that 42% of patients were treated with oral hypoglycemic drugs alone (sulfonylureas or glinides), 46% with insulin therapy and the remaining 6% with combined therapy.

About the clinical symptoms, 40% of patients presented autonomic symptoms, 8% dizziness, 20% and 60% presented respectively focal neurologic deficit and altered consciousness until coma. In these conditions the clinician suspected acute neurological events, in particular ischemic stroke, and requested CT examinations and specialist consultations, which could be avoided if a simple blood glucose control was performed.

Severe hypoglycemia was associated with falls at home in 22% of cases and a patient reported a fracture. At the medical triage, the most frequently emergency code assigned was the red code (52%), which identifies the most urgent treatment needed.

Table 2 show main predictors of hospitalization. Hospitalization rates occurred in 62% of patients, whereas in-hospital deaths occurred in 4% of cases. One patient died in the emergency room, it was an elderly man who presented with an extremely low blood

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glucose value equal to 0.56 mmol/L (10 mg/dL), while the other patient, suffering from advanced cancer, died in the ward after a 4-day hospital stay.

The average length of hospital stay was 17.06 ± 10.09 days. No risk factors were statistically significant correlated with hospitalization. Most of the hospitalizations were needed for the frailty of the elderly diabetic patients and their comorbidities, rather than the episode of severe hypoglycemia.

**Table 1. Main comorbidities and clinical characteristics**

| Variable | N = 50 |
|---|---|
| Age, years, median | 80.78 |
| Sex, Female, n (%) | 17 (34) |
| Glycemia, mmol/L, median | 3.1 |
| Hypertension, n (%) | 39 (78) |
| Dyslipidemia, n (%) | 23 (46) |
| Chronic kidney disease, n (%) | 27 (54) |
| Respiratory disease, n (%) | 10 (20) |
| Malignancy, n (%) | 8 (16) |
| Atrial fibrillation, n (%) | 19 (38) |
| Coronary artery disease, n (%) | 21 (42) |
| Previous ischemic stroke, n (%) | 13 (26) |
| Infection in progress, n (%) | 17 (34) |
| Antidiabetic drugs | |
| Sulfonylureas or glinides, n (%) | 21 (42) |
| Insulin therapy, n (%) | 23 (46) |
| Combined therapy, n (%) | 3 (6) |
| Autonomic symptoms, n (%) | 20 (40) |
| Dizziness, n (%) | 4 (8) |
| Focal neurological deficit, n (%) | 10 (20) |
| Altered consciousness, n (%) | 30 (60) |

## 5. Discussion

In this single-center study, we identified a total of 50 cases of severe hypoglycemia over a period of 1 year in diabetic patients requiring ED cares. However, it is important to underline that our results represent only a little part of a serious clinical health problem because the patients usually treat most of their mild or moderate hypoglycemic events without any assistance. Therefore, we could assume that our results may largely underestimate the prevalence of symptomatic hypoglycemia in people with established diabetes.

No patient was being treated with new antidiabetic drugs, while they were taking sulfonylureas or glinides, insulin or both. The insulin-releasing action of these drugs can be persistent at low glucose levels, which would lead to the development of hypoglycemia, making these drugs an undesirable choice for older diabetic patients [21].

In our study we observed that hospitalization was necessary for elderly diabetic patients with various comorbidities. Episodes of severe hypoglycemia were promptly and correctly treated in the ED, with normalization of blood glucose values. However, patients often could not be discharged due to their frailty and poor home care. Therefore, it seems from our study that episodes of severe hypoglycemia in elderly diabetic patients indicate a precarious clinical stability, resulting in the need for hospitalization.

## 6. Limitations

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 September 2022 doi:10.20944/preprints202209.0153.v3

Our work had some limitations. The retrospective nature of the study affected the numerical non-uniformity and baseline characteristics of the two comparison groups. Some data were not available for analysis, as they could not be obtained from the consulted sources. Changes in patterns of presentations to EDs have been reported during COVID-19 lockdowns, including reduced numbers of patients with certain high acuity conditions, such as acute coronary syndrome (ACS) and stroke [22, 23]. Therefore, we cannot exclude that the same phenomenon affects cases of severe hypoglycemia, leading to underestimation the prevalence of symptomatic hypoglycemia.

**Table 2. Main predictors of hospitalization**

| Variable | Hospitalization | | OR | OR CI 95% | Chi square | p value |
|---|---|---|---|---|---|---|
| | No = 19 | Yes = 31 | | | | |
| **Sex** | | | | | | |
| Male | 14 (42.4%) | 19 (57.6%) | 0.485 | 0.506 - 6.179 | 0.806 | 0.369 |
| Female | | | | | | |
| **Age (years)** | | | | | | |
| Mean | 72.7 | 80.4 | | | -1.915* | 0.126 |
| < 80 | 11 (45.8%) | 13 (54.2%) | 1.904 | 0.599 - 6.054 | 1.202 | 0.273 |
| ≥ 80 | 8 (30.8%) | 18 (69.2%) | | | | |
| **Kidney failure** | | | | | | |
| No | 9 (39.1%) | 14 (60.9%) | 1.093 | 0.348 - 3.435 | 0.023 | 0.879 |
| Yes | 10 (37.0%) | 17 (63.0%) | | | | |
| **Glycemia (mmol/L)** | | | | | | |
| < 3.1 | 9 (37.5%) | 15 (62.5%) | 0.960 | 0.306 - 3.012 | 0.005 | 0.944 |
| ≥ 3.1 | 10 (38.5%) | 16 (61.5%) | | | | |
| **Autonomic symptoms** | | | | | | |
| No | 14 (46.7%) | 16 (53.3%) | 2.625 | 0.759 - 9.076 | 2.391 | 0.122 |
| Yes | 5 (25.0%) | 15 (75.0%) | | | | |
| **Dizziness** | | | | | | |
| No | 16 (34.8%) | 30 (62.5%) | 0.178 | 0.017 - 1.851 | 2.526 | 0.112 |
| Yes | 3 (75%) | 1 (25%) | | | | |
| **Focal neurologic deficit** | | | | | | |
| No | 17 (42.5%) | 23 (57.5%) | 2.957 | 0.556 - 15.729 | 1.719 | 0.190 |
| Yes | 2 (20.0%) | 8 (80.0%) | | | | |
| **Altered consciousness** | | | | | | |
| No | 9 (45.0%) | 11 (55.0%) | 1.636 | 0.512 - 5.325 | 0.693 | 0.405 |
| Yes | 10 (33.3%) | 20 (66.7%) | | | | |
| **Fall** | | | | | | |
| No | 13 (33.3%) | 26 (66.7%) | 0.417 | 0.107 - 1.625 | 1.639 | 0.201 |
| Yes | 6 (54.5%) | 5 (45.5%) | | | | |
| **Triage category** | | | | | | |
| Semi-urgent | 0 (0.00%) | 1 (100%) | | | 4.369 | 0.224 |
| Urgent | 5 (71.4%) | 2 (28.6%) | | | | |
| Very urgent | 5 (31.3%) | 11 (68.7%) | | | | |
| Emergency | 9 (34.6%) | 17 (65.4%) | | | | |
| **Observation Unit** | | | | | | |
| No | 14 (40.0%) | 21 (60.0%) | 1.333 | 0.375 - 4.742 | 0.198 | 0.656 |
| Yes | 5 (33.3%) | 10 (66.7%) | | | | |
| **Death** | | | | | | |
| No | 17 (36.2%) | 30 (63.8%) | 0.567 | 0.033 - 9.650 | 0.158 | 0.691 |
| Yes | 1 (50.0%) | 1 (50.0%) | | | | |

OR: odds ratio; CI: confidence interval; * Student's t

## 7. Conclusions

Severe hypoglycemia is a common problem in older people with diabetes. Aging changes the cognitive and symptomatic responses to hypoglycemia, increasing the risk of unawareness or severe episodes of hypoglycaemia. Although hypoglycemia in the elderly is the most common complication of tight glycemic control, multiple comorbidities such as chronic kidney failure, heart disease, malnutrition and polypharmacy can increase the risk of this complication and the need for hospitalization.

 doi:10.20944/preprints202209.0153.v3

**Author Contributions:** Conceptualization, L.P. and E.M.; data curation, G.L.; methodology, L.P.; supervision, M.A.; validation, M.A.; writing-original draft, L.P. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** This study was also approved by the local Ethics Committee [45-2022-OSS_ALTRO-MN17].

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** Data are available on request from the corresponding author.

**Conflicts of Interest:** The authors declare they have no conflict of interest.

 doi:10.20944/preprints202209.0153.v3

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