DOI:
10.1016/j.ienj.2018.10.005

Document Version
Peer reviewed version

Title page

Title Characteristics of patients treated for severe hypoglycaemia in emergency care settings - analysis of routinely collected data

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Word count 4,423

Number Tables 3

Abstract

Objective: Severe hypoglycaemic events (SHE) commonly require emergency care. This study investigates the presentation of patients with SHE to a single Swiss emergency service, including pre-hospital care with emergency medical services (EMS) and emergency department (ED) presentations.

Method: Retrospective analysis of routinely collected data by the EMS and ED during 2014. All adult patients with diabetes type 1 or type 2 with SHE were included in the analysis.

Results: 43 SHE were recorded in 38 patients with diabetes. Mean age of all patients was 65 years (*SD*±17.51), 54% (*n*=23) were men, 55.8% (n=24) were living in a relationship, and 54.8% (n=23) were diagnosed with type 2 diabetes. Of the 43 episodes, 65% (*n*=28) of the presentations used EMS and were then taken to the ED, 28% (*n*=12) involved contact with the EMS only, and 7% (*n*=3) were seen by the ED but did not use EMS. Patients seen by the EMS only (*n*=12) were younger compared to those admitted to ED (*n*=28); *Md* 54 years vs *Md* 72 years; *U*=98; *p*=.039. The same age difference was similar between patients in the ED setting discharged home (*n*=11) and with in-patients (*n*=20); *Md* 61 years vs. *Md* 79 years; *U=51*; *p*=.013.

Conclusions: People most likely to suffer a SHE were men, those living with a partner, over 65 years old, and living with type 2 diabetes. Younger patients treated by EMS at home tended to remain at home, in contrast to the older patients who were admitted to hospital. This was also true for the ED where older people in particular became in-patients after such an event. Elderly care specialist brief interventions conveyed by EMS and ED healthcare professionals might be of value to prevent further SHE. Validating these findings in multiple emergency settings is warranted to support the delivery of targeted interventions.

Manuscript

INTRODUCTION

Diabetic hypoglycaemia, defined as a glucose level of 3.9 mmol/L or lower [1], is the most frequent and acute complication of treatment with antidiabetic medication [2, 3] and the major limiting factor in glycaemic management [4]. Further, hypoglycaemia is a clinical problem in both, patients with type 1 diabetes (T1DM) and type 2 diabetes (T2DM) [5]. Studies describe that patients with T1DM on average experience 43 hypoglycaemic events per year and patients with T2DM experience 16 events annually [6, 7].

While the initial symptoms of hypoglycaemia warn patients of an hypoglycaemic event occurring, the symptoms can vary considerably between individuals [8]. The symptoms of hypoglycaemia can be categorised as autonomic symptoms (sweating, palpitations, shaking, hunger), neuroglycopenic symptoms (confusion, drowsiness, odd behaviour, speech difficulty, incoordination) and unspecific symptoms (headache, nausea) [8, 9]. In severe cases, hypoglycaemia can lead to seizure, coma and death [6, 8-10]. Hypoglycaemic episodes are typically characterized as either non-severe or severe, according to whether the person with diabetes can manage the event alone, or whether the hypoglycaemia event is associated with severe cognitive impairment requiring external assistance for recovery [1, 11]. So, while non-severe episodes of hypoglycaemia are treated effectively by the patients themselves, severe hypoglycaemic events (SHE) are treated by family members and friends but are also the most common reason for people with diabetes requiring emergency medical assistance [12]. Prior studies on SHE emergency service treatment have largely focused on trends and incidence rates in patients with diabetes predominantly in the U.K. and North America. A U.S. national trend survey, showed that admissions for SHE increased by 11.7% over a 12-year period [13]. However, they did not include emergency medical services (EMS) calls not leading to emergency department (ED) admission, losing vital information on this specific subgroup as shown by a U.K. based survey [12]. Therefore, there is a high risk for underestimating the trend of SHE and hence the overall burden for patients, families and friends. Nevertheless, incidence rates of SHE treated by emergency services have been reported to be as high as 11.5 and 11.8 events per 100 patient-years for T1DM and T2DM

patients treated with insulin, respectively [14]. Other identified risk factors for SHE in this study included age, duration of diabetes, and socioeconomic status. Unfortunately, the study did not report on patients with SHE treated by family and friends at home or at their work place, resulting again in a possible underestimation of SHE. Furthermore, the results do not reveal patterns of the SHE occurrence such as seasonal variation, time and place of incident, or whether patients treated at home for SHE varies from those treated at the ED, or those with in-patient admission. Therefore, this present study aims to investigate the presentation of patients with SHE to Swiss emergency services, including pre-hospital care with EMS and ED presentations to ascertain:

- the number of patients requiring emergency medical treatment,
- the demographic and clinical characteristics of presenting patients.

This study is part of an extended study whose aim is to identify opportunities to intervene during emergency care provision as well as the development of brief interventions and resources for use by healthcare professionals in this setting to better support self-management and prevent subsequent emergency presentations of patients with SHE.

METHOD

This was a retrospective electronic medical record review of the entire population of adult patients (≥18 years) with T1DM or T2DM who were treated by a single Swiss emergency service, including pre-hospital care with emergency medical service (EMS) and emergency department (ED) between 1 January and 31 December 2014 for hypoglycaemia.

Participants

Eligible medical records were identified by either the international classification of diseases, 10th revision, German modification (ICD-10-GM) codes or by initial glucose meter reading below 4mmol/L and the diagnosis of a hypoglycaemia. Two data sources were searched for eligible patient records - EMS and ED electronic medical records. Excluded patients were those with SHE occurred

after admission and those with a documented refusal to use their data for research. All hypoglycaemic events were classified as severe, as they required external assistance for recovery.

Setting

The cantonal hospital of Winterthur is one of the ten largest hospitals in Switzerland and is based in the German speaking part of the country. Five hundred and thirty beds provide medical care for a population of approximately 200,000. In 2014, there were 8,415 EMS calls and 37,095 ED presentations [15].

Data collection

Study data were abstracted from the electronic medical records onto study specific case report forms. To avoid bias and increase inter-rater-reliability following data abstraction strategies were appointed: 1) the report form was piloted prior to full study rollout by the first author; 2) data in the EMS and ED were collected by the first author and a second data abstractor. The second person received a training by the first author for the data abstraction; 3) distinct variable definitions and inclusion and exclusion criteria were set; 4) distinct rules regarding the management of missing or conflicting data were established and 5) ten percent of the abstracted data in random samples were double checked by the other data abstractor. After the completed data entry all data was double-checked for missing or wrong data entry to ensure high data entry quality by the first author.

The information recorded reflects the following categories: administrative data (e.g. type of referral, month, time of day and place the event occurred), demographic data (e.g. gender, age and marital status), and clinical data (e.g. initial glucose meter reading, diabetes type, diabetes duration, and diabetes medication). The data collection aimed at aggregating detailed information on patients' presentation in order to investigate patterns of the SHE occurrence as in e.g. seasonal variation, time and place of incident and social support.

Statistical analysis

All statistical analyses were carried out using SPSS version 24. To outline the characteristics of the participants, descriptive statistics was used. Continuous measures are expressed as mean and standard deviation, except for variables with non-normal distribution that are expressed as median (interquartile range). Discrete variables are reported as count and/or percentage. Group comparison was performed with the t- test and Mann–Whitney U, where appropriate.

Ethics

The study was approved by the ethical committee of the Canton Zurich, Switzerland (KEK-ZH-Nr: 2015-0276).

RESULTS

In the 12 months (January to December 2014), 43 severe hypoglycaemia-related events were recorded in 38 patients with diabetes.

Administrative data

The prevalence rate of patients with SHE requiring emergency medical assistance through EMS was 0.5%, and 0.1% in patients seen by the ED. Of the 43 episodes, 65% (*n*=28) of presentations were treated by EMS and were then taken to the ED, 28% (*n*=12) involved treatment with the EMS at home only, and 7% (*n*=3) were treated by the ED but not the EMS. In 90% of the cases, EMS were called out to the patient's home and 10% attended to patients in a public place. Family members, friends or neighbours made 70% (*n*=28) of the emergency calls. A further 15% were made by home care nurses (*n*=6), and another 15% of the calls were made by police (*n*=3), work colleagues (*n*=3), and strangers (*n*=1). Thirty percent of referrals to EMS and ED occurred in the afternoon and 30% at night-time (*n*=26), followed by 24% during the evening (*n*=10) and 16% in the morning (*n*=7; X^2=2.302; *p*=.537). In regard of seasonal variation: 30% of the SHE (*n*=13) took place during autumn, 28% (*n*=12) during spring, 26% (*n*=11) in summer, and 16% (*n*=7) during the winter months (X^2=3.967; *p*=.272).

Demographics and clinical characteristics

Of the 43 hypoglycaemic-related events, 54% (*n*=23) were experienced by male patients. The median age was 65.1 years (*SD*±17.51). Divided into age groups, 2% (*n*=1) were between 1 and 19 years, 5% (*n*=2) between 20 and 29 years, 37% between 40 and 64 years (*n*=16) and 56% (*n*=24) older than 65 years. Overall, 35% (*n*=15) of the 43 SHE were 75 years or older. Regardless, whether patients were treated at home by the EMS or whether they were treated at the ED, the majority were married or living in a partnership (treated by EMS only *n*=6; 50% vs. treated at the ED *n*=18, 58%). The mean years since patients with T1DM had their diabetes diagnosed was 20.5 years (*SD*±10.23), respectively 16 years (*SD*±10.02) in patients with T2DM. Among the 31 patients treated at the ED, all patients were on insulin. The current body mass index based on data in 23 cases, indicated that 53% (*n*=17) were within the normal BMI range, 23% of the patients were overweight (*n*=7) and 25% (n=8) were obese. The detailed patient demographics and medical data is presented in table 1.

Table 1: Demographic and medical data

	Sample n=43	EMS and ED n=28	EMS n=12	ED n=3
Male sex, *n (%)*	23 (53.5%)	15 (53.6%)	6 (50.0%)	2 (66.7%)
Age (years), *M (±SD, min-max)*	65.1 (±17.51, 18-90)	68.36 (±16.35, 31-90)	55.0 (±18.50, 18-79)	75.0 (±6.55, 69-82)
Relationship status, *n (%)*				
Living alone	19 (44.2%)	12 (42.9%)	6 (50.0%)	1 (33.3%)
Living in a relationship	24 (55.8%)	16 (57.1%)	6 (50.0%)	2 (66.7%)
Occupational status, *n (%)*				
Employed	11 (25.6%)	8 (28.6%)	3 (25.0%)	0 (0%)
Unemployed	7 (16.3%)	2 (7.1%)	5 (41.7%)	3 (100%)
Retired	24 (55.8%)	17 (60.7%)	4 (33.3%)	0 (0%)
Disabled	1 (2.3%)	1 (3.6%)	0 (0%)	0 (0%)
Nationality, *n (%)*				
Swiss	30 (76.7%)	20 (80.0%)	10 (90.9%)	0 (0%)
Other	9 (23.7%)	5 (20.0%)	1 (9.1%)	3 (100%)
Diabetes type, *n (%)*				
Type 1	19 (45.2%)	11 (39.3%)	8 (72.7%)	0 (0.0%)
Type 2	23 (54.8%)	17 (60.7%)	3 (27.3%)	3 (100.0%)
Diabetes since (years), *M (range)*[1]	18.14 (46)	16.58 (46)	22.00 (13)	17.00 (n/a)
Type 1	20.54 (35)	17.17 (35)	23.43 (11)	*No data*
Type 2	16.07 (43)	16.31 (43)	12.00 (n/a)	17.00 (n/a)
Diabetic medication, *n (%)*				
Antihyperglycaemic agents	3 (7.3%)	1 (3.6%)	0 (0%)	2 (66.7%)
Insulin	29 (70.7%)	18 (64.3%)	10 (100%)	1 (33.3%)
Combination	9 (22.0%)	9 (32.1%)	0 (0%)	0 (0%)
$HbA1_{c,}$ (mmol/L), *M (±SD, min-max)*	7.70 (±1.24, 5.7-9.7)	7.84 (±1.29, 5.7-9.7)	7.54 (±1.12, 6.9-9.6)	7.45 (±2.05, 6.0-8.9)
BMI (kg/m^2), *M (±SD, min-max)*	26.19 (±4.78, 19.4-35.8)	26.97 (±5.20, 19.4-35.8)	23.95 (±2.83, 20.5-30.0)	27.66 (±5.85, 23.2-34.3)

[1] Data presented in median and range as sample sizes are very small and therefore skewed so standard deviations are not reported.

Hypoglycaemic presentation and treatment in EMS

The patients treated by EMS presented with following symptoms: 88% (*n*=35) had at least one documented neuroglycopenic symptom, followed by 75% (*n*=30) autonomous symptoms, 50% (*n*=20) serious symptoms and 8% (*n*=3) unspecific symptoms. The 40 patients had a mean initial glucose meter reading of 2.1mmol/L (*SD*±0.85). Patients with T1DM showed a mean initial glucose meter reading of 2.15 mmol/L (*SD*±0.99) compared to patients with T2DM; 2.05 mmol/L (*SD*±0.74, *U*=187; *p*=.945). A comparison between patients treated at home by EMS (*n*=12) and those additionally admitted to ED (*n*=28) showed no statistical difference in initial glucose meter reading, gender, type of diabetes and diabetic medication. However, EMS patients discharged (i.e. treated at home and not taken to the ED) were younger and had a median age of 54 years vs. EMS patients discharged to ED with a median age of 72 years; *U*=98; *p*=.039. Details are presented in table 2. In 59% of the events (*n*=10) patients were accompanied by a significant other when discharged from EMS to everyday life. Patients transferred to ED were escorted in 41% (*n*=7) by their family members. In 23 cases, companionship was not described.

Table 2: Difference between EMS patients discharged to everyday life or transferred to ED

	Treated at home n=12	Transferred to hospital n=26	Test statistics	p-value*
Male gender, *n* (%)	6 (50.0)	15 (53.6)	X^2=.043	*p*=1.000
Age (years), *Md (IQR)*	53.50 (27)	72.00 (25)	*U*=98	*p*=.039*
Initial glucose level (mmol/L), *Md (IQR)*	2.0 (1.05)	2.1 (.58)	*U*=162	*p*=.873
Diabetes type *n (%)*			X^2=3.535	*p*=.082
DM type 1	8 (72.7)	11 (39.3)		
DM type 2	3 (27.3)	17 (60.7)		
Diabetic medication *n (%)*			X^2=4.847	*p*=.105
OAD	0 (0)	1 (3.6)		
Insulin	10 (100)	18 (64.3)		
Combination	0 (0)	9 (32.1)		

* Significant $p<.05$

Hypoglycaemic presentation and treatment in ED

Among all the patients treated in ED, 39% (*n*=12) presented with at least one documented neuroglycopenic symptom, followed by 36% (*n*=11) autonomous symptoms, and 16% (*n*=5) unspecific symptoms. No patients showed serious symptoms. The 31 patients had a mean initial glucose meter reading of 4.18mmol/L (*SD*±2.79). Patients with T1DM showed a mean initial glucose meter reading of 5.68 mmol/L (*SD*±3.74) compared to patients with T2DM; 3.35 mmol/L (*SD*±1.70). However, 28 of these patients had received an earlier treatment by the EMS. In the three patients admitted directly to the ED, the mean initial blood glucose meter readings were 2.10 mmol/L (*SD*±0.51). In 20 cases, ED presentation led to admission as an in-patient with an average stay of 5 days (*SD*±3.55). A comparison between patients discharged (*n*=11) and in-patients (*n*=20) showed no difference in initial glucose meter reading, gender, type of diabetes and diabetic medication. However, ED patients discharged home were younger and had a median age of 61 years vs. ED patients with in-patient admission and a median age of 79 years; *U=51*; *p*=.013. Details are presented in table 3.

Table 3: Difference between ED patients discharged home or with in-patient follow-up

	Discharged home n=11	Inpatient treatment n=20	Test statistics	p-value*
Male gender, *n (%)*	5 (45.5)	12 (60.0)	X^2=.606	*p*=.477
Age (years), *Md (IQR)*	61.00 (24)	78.75 (19)	*U*=51	*p*=.013*
Initial glucose level (mmol/L), *Md (IQR)*	4.0 (3.50)	3.1 (3.93)	*U*=101	*p*=.722
Diabetes type *n (%)*			X^2=2.706	*p*=.132
DM type 1	6 (54.5)	5 (25.0)		
DM type 2	5 (45.5)	15 (75.0)		
Diabetic medication *n (%)*			X^2=1.981	*p*=.552
OAD	0 (0)	3 (15.0)		
Insulin	7 (63.6)	12 (60.0)		
Combination	4 (36.4)	5 (25.0)		

* Significant *p*<.05

Patients with frequent SHE

Among the five patients who suffered from SHE more than once in this period, one female suffered from five SHE, and the other four patients (two females and two males) from two events each. Their mean age was 67.6 years (*SD*±21.85). Two patients suffered from T1DM and three from T2DM, all were taking insulin. All 13 events were treated by EMS at the patients' home and in nine events, they were further treated at the ED. In six events, ED presentation led to hospital admission with an average stay of 3 days (*SD*±32.6). While one patient died, the above-mentioned female was referred for follow-up treatment to a psychiatry after suffering her fifth SHE.

DISCUSSION

Building on the knowledge of previous publications, this is the first study investigating numbers and characteristics of patients with diabetes presenting with SHE to a Swiss emergency service including the patterns of the SHE occurrence as in seasonal variation, time and place of incident. Further, the study examined the differences of patients treated at home, compared to those treated at the ED, or those with in-patient follow-up.

Our study results showed that the largest single group of people affected by SHE were male, over 65 years of age, living with a partner and a diagnosis of type 2 diabetes for over a decade. However, when examining patients with frequent SHE, women were more prominent. This indicates that women should also be regarded vulnerable as their life spans are longer and they at some point may be having to cope with health-related complications on their own. Further, although the home environment could be regarded as a safe place and most patients were living with significant others, 90% of the SHE occurred at home. In addition, the results indicated that over a quarter of patients were treated at home by EMS and were not referred to the ED, which potentially resulted in a heavy burden on family members. This result highlights the importance of healthcare professionals including significant others in the provision of hypoglycaemic specific preventive as well as problem-solving approaches.

A second important finding is, that the incidence of patients with diabetes treated for SHE in this single Swiss hospital is low indicating that EMS and ED staff rarely care for this specific population. This may limit their knowledge of referring agencies for follow up care. The study also showed that younger patients treated by EMS at home tended to remain at home in contrast to the older patients who were admitted to hospital. This was also true for the emergency department where older people in particular (>72 years) became in-patients after such an event. The overall finding, that old age is a risk factor for SHE has been confirmed by other studies [16]. They state, that the increased risk for SHE in the older population could be due to counter regulatory responses, aged related impairments in renal and hepatic functions, and a prolonged illness duration. Additionally, recent published evidence suggests that a substantial proportion of older people with diabetes are potentially overtreated [17-19]. Further, autonomic symptoms are diminished and symptom intensity is low overall in older people [20]. Older patients with diabetes suffering from SHE can therefore be considered particularly vulnerable and frail as also stated in other studies [21].

The severity of the SHE measured by blood glucose showed an equal distribution between the two diabetes types requiring emergency services. However, more patients with T2DM were in need of healthcare professional's treatment than patients with T1DM. This finding was also found by Elwen and colleagues. They argued, that the majority of SHE among T1DM in the community are treated by friends or family members and are therefore not in need of emergency service treatments. As a result, the episodes treated by emergency services are those, which could not be successfully dealt with by the individuals, their family members or friends [22]. This indicates, that patients with T2DM in the present study may not be receiving the education needed while adjusting to new medical regimes (e.g. new on take of insulin) and again highlights the importance of including family members and significant others in learning about consequences of medical adjustments and specific problem-solving skill.

In the present study, the mean diabetes duration was over a decade. Further, nearly all the patients were prescribed insulin, regardless of their diabetes type. Donnelly and colleagues highlight, that patients with T2DM on insulin for more than 10 years are at risk for hypoglycaemic events. They

explain, that this subgroup of patients may suffer from a counter regulatory hormonal deficiency related to pancreatic beta-cell failure [7]. In addition, blood glucose control in patients with diabetes is reportedly influenced by seasons. Our study did not find any statistical difference of seasonal variations. However, the study by Tsujimoto and colleagues showed that in the T1DM group, severe hypoglycaemia occurred significantly more often in the summer than in the winter (35.2% in summer vs 18.2% in winter, p=0.01). In the T2DM group, the occurrence of severe hypoglycaemia and the $HbA1_c$ levels did not differ significantly among the seasons [23]. Nonetheless, these findings have to be considered while caring for patients with cultural differences. For example for patients with diabetes fasting during the Ramadan months, SHE is a serious health risk [24]. In Europe, over the next ten years Ramadan will take place in the summer months, and patients with diabetes need education appropriate support [25].

Study strengths and limitations

This study employed high quality survey and chart review methods and our data collection was based on a standard data collection form [26]. We studied people with diabetes in real world setting and included EMS calls not leading to ED admission. Therefore, we added evidence for treatment outside the tight constraints of a clinical setting and the results are more representative of usual severe hypoglycaemic events and give a detailed description of those patients treated at home compared to those treated at the ED.

However, this study has some limitations that should be accounted for when interpreting the results. First, there are limitations to medical record reviews, as the data is originally not recorded for research purposes and, therefore, may be lacking in quality and quantity [26]. To reduce this bias, valid methods were applied (e.g. including multiple sources of EMS and ED information and double-checking the data). However, there is a loss of some clinical history data from patients being treated by the EMS and ED (e.g. duration of patients on insulin) that would have led to a more differentiated description of the patient's characteristics and their risk factors for SHE. Second, as Switzerland has no national diabetes registry and there is no access to population data, a point of prevalence cannot be reported.

Implications for practice and research

Based on our own and previous study results, the people most likely to suffer a SHE are men, living with a partner, and are over 65 years old. Furthermore, they are living with a diabetes type 2 for more than 10 years. These findings help to identify patients most at risk and who would benefit from preventive interventions. SHE are under-recognised medicine-related adverse events in older patients and are often linked to other disorders [20]. As the older population grows rapidly, this is an important finding for future interventions to be developed in order to minimize hospital admissions. Especially elderly care specialist brief interventions conveyed by EMS and ED healthcare professionals might be of value to prevent further SHE. EMS and ED healthcare professionals are key persons involved in the treatment and management of these patients [27]. But also, as the majority of the SHE occurred at the patient's home in the presence of family member, it is vital to include those in any self-management and problem-specific approaches, as brief interventions are. Our findings show, that the involvement of significant others or family members is not consistently being recorded by healthcare professionals and not being recognized as a valuable resource. Findings from a meta-analysis indicated that social support from family members is significantly correlated with diabetes self-care, notably for glucose monitoring [28]. However, a recently published systematic literature review highlighted the lack of evidence related to brief interventions in diabetes and especially in the brief opportunistic environments of ED where people with diabetes attend frequently [29].

CONCLUSION

This retrospective analysis of routinely collected data has highlighted that especially elderly men with diabetes type 2 are most likely to suffer from SHE. Future research needs to be conducted in order to understand what are the patients' needs and how best to prevent future SHE. A better understanding has to be gained about the different stages patients and their family members' experience - from the SHE to the hospital admission and its discharge as well as the follow-up care. This will be the foundation for the development of brief interventions for affected patients and thus enhance diabetes quality care.

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Acknowledgment

The authors thank the representatives of the Cantonal hospital of Winterthur for supporting the study as well as the two Master in Nursing Science students Mrs Daniela Suter and Mrs Nina Karrer for their support during the data collection phase.

Funding

This study was supported by the Nursing Science Foundation Switzerland.