Factors associated with hospital-acquired hypoglycaemia among older people with type 2 diabetes

Nataliya Shaforost, Donna Jornsay

Hypoglycaemia remains a major obstacle for achieving appropriate glycaemic control among hospitalised older people with type 2 diabetes. The aim of this study was to identify factors contributing to hospital-acquired hypoglycaemia, both mild and severe, among this population. A retrospective chart review of 229 inpatients aged ≥65 years with type 2 diabetes at a community hospital in Queens, New York, was conducted between January 2013 and April 2014. A descriptive cross-sectional design was utilised to explore possible factors contributing to hypoglycaemia. Hospital-acquired hypoglycaemia was associated with elevated blood urea nitrogen and serum creatinine levels, location within the hospital, healthcare professional work shift, and day of hospital stay. Given these findings, a number of recommendations to improve hypoglycaemia risk can be made.

As the average age of the population has grown, so too has the proportion of hospitalised people with diabetes who are over the age of 65 years. Current guidelines for the management of diabetes in inpatients are based on the fact that poor glycaemic control worsens patient outcomes and extends hospital length of stay (Mendez et al, 2013). Hypoglycaemia remains a major obstacle to achieving targeted glycaemic control for all age groups and particularly for older people (Cryer, 2002). Hypoglycaemia occurs in all settings and is associated with an increased risk of fall-related events (Kachroo et al, 2015).

Hypoglycaemia is generally defined as an abnormally low capillary blood glucose level of <3.9 mmol/L, and is a condition proven to cause multisystem damage that may result in death (Cryer et al, 2009). Among older people with diabetes, hypoglycaemia carries a particularly high risk of acute and even fatal events (Seaquist et al, 2013). It has also been shown to significantly increase both length of hospital stay and mortality rates (Turchin et al, 2009).

In hospitalised older people with type 2 diabetes, hypoglycaemia can become severe (Pratley et al, 2014). Severe hypoglycaemia has been linked to the incidence of dementia in older adults and can trigger behavioural changes, diminish cognitive function and lead to traumatic injury, seizures, unconsciousness and death (Vexiau et al, 2008; Pratley et al, 2014). Currently, in the US hospital setting, the incidence of hypoglycaemia is said to be as high as 10% among people with type 2 diabetes (Boucai et al, 2011).

The intrinsic factors associated with older people that contribute to the high incidence of hypoglycaemia are polypharmacy, depression, dementia and stroke (Braithwaite et al, 2004), and multiple comorbidities, such as chronic renal or hepatic deficiency and congestive heart failure (Bramlage et al, 2012). The known iatrogenic hospital environmental factors impacting hypoglycaemia rates are asynchrony of food delivery and insulin administration, nutritional

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Article points

1. Hypoglycaemia remains a major obstacle to achieving appropriate glycaemic control in older adults with type 2 diabetes.
2. There is no clear consensus on factors contributing to hypoglycaemia specifically amongst older hospitalised people.
3. The objective of this study was to assess the relationship between hypoglycaemia among 229 older inpatients and the various factors that have previously been identified in the general adult diabetes population.
4. Elevated blood urea nitrogen and serum creatinine levels, hospital unit, healthcare professional work shift and the day of hospital stay were all positively associated with hypoglycaemia in this age group.

Key words

- Hospital
- Hypoglycaemia
- Inpatient care
- Older people
- Type 2 diabetes

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Details can be found at the end of the article.

Page points

1. The aim of this study was to determine the factors associated with hospital-acquired hypoglycaemia in older people with type 2 diabetes.
2. This was a retrospective chart review of people who had a documented episode of hypoglycaemia whilst admitted to the general medical–surgical units of a 288-bed community hospital in Queens, New York.
3. A total of 229 older people (mean age, 78 years) were evaluated. Severe hypoglycaemia (capillary blood glucose level, <2.2 mmol/mol) occurred in 18.3% of this cohort.

interruptions, and nil-by-mouth status. Sliding-scale insulin use (Maynard et al, 2008; Rubin et al, 2011), although no longer recommended, is a significant contributor to inpatient hypoglycaemia, as is previous hypoglycaemia during the same hospital stay (Farrokhi, 2012).

Elliott et al (2012) analysed severe hypoglycaemia in hospitalised adults with type 1 and type 2 diabetes and concluded that identification of the factors associated with hypoglycaemia could lead to the prevention of more than 60% of severe hypoglycaemic events. While some of these findings could be useful in developing preventative strategies for hypoglycaemia in the general inpatient population, there still is no clear consensus on factors contributing to hypoglycaemia explicitly among older hospitalised patients.

The purpose of this study was to investigate the contributing factors to hypoglycaemia specifically among older inpatients with type 2 diabetes. The study aimed to assess the relationship between the hypoglycaemic events and the numerous factors previously studied in adults of unspecified age. These factors include medical provider education and speciality, patient literacy, presence of liver or kidney disease, blood urea nitrogen (BUN) level, serum creatinine level, type of oral antidiabetes medication, type of insulin, sliding-scale insulin use, history of hypoglycaemia, length of hospital stay, patient location within the hospital, and healthcare provider work shift (Durán-Nah et al, 2008; Vexiau et al, 2008; Moen et al, 2009). Following the work of Elliott et al (2012), who were able to demonstrate a reduction in the rate of hypoglycaemia by identifying and testing the factors associated with it, our aim was to differentiate the associated factors specifically in older people. Knowledge of these factors will allow diabetes providers to work towards the reduction and prevention of hypoglycaemia in this vulnerable population.

Study design and methods

This retrospective chart review of people admitted to the general medical–surgical units of a 288-bed community hospital in Queens, New York, between 1 January 2013 and 1 April 2014 was conducted to identify causes of and risk factors for hypoglycaemia. The study was approved by the institution's ethical review board (IRB #14-118A).

Sample selection

A total of 1172 medical records with documented episodes of hypoglycaemia among adults admitted to the hospital general wards were reviewed, and 229 subjects were identified for the study based on the inclusion criteria. Inclusion criteria consisted of men and women aged ≥65 years who were admitted to the hospital with a history of type 2 diabetes and who were treated for hyperglycaemia with oral antidiabetes agents and/or insulin prior to the event of hypoglycaemia. Data on all episodes of capillary blood glucose levels <3.9 mmol/L were obtained from the hospital's electronic medical record. Severe hypoglycaemia was defined as a capillary blood glucose level <2.2 mmol/L. Study exclusions were people with an episode of hypoglycaemia in the first 24 hours of admission to the hospital and those with a history or new diagnosis of pancreatitis or pancreatic tumours.

Data collection and analysis

Hard copies of participants' medical records were obtained and the following data were recorded: demographics, type of hospital unit, healthcare provider shift, history of type 2 diabetes, history of kidney disease, capillary blood glucose levels, serum creatinine levels, BUN levels, HbA_{1c} levels and diabetes medications.

Data were analysed using SPSS version 22 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were generated for all variables, in addition to chi-squared analysis and Pearson product-moment correlation coefficients to determine the most significant variables.

Results

A total of 229 people who had a capillary blood glucose level under 3.9 mmol/L during their hospital stay were identified from the review of patient charts. The average age of the participants was 78 years, with the majority being ≥75 years of age (*n*=136 [59%]; *Table 1*). The average blood glucose level was 2.8 mmol/L, with 42 people (18.3%) having a level of <2.2 mmol/L. There was no significant correlation between HbA_{1c} levels and hypoglycaemia rate.

Table 1. Characteristics of patients with a hypoglycaemic episode (*n*=229).

Patient characteristic	*n*/mean	Range
Age (mean; years)	78.1 (SD, 8.4)	65–99
Age group:		
<75 years	93 (40.6%)	
≥75 years	136 (59.4%)	
Gender (female)	117 (51.1%)	
Notification of diabetes on admission	195 (85.2%)	
History of kidney failure	102 (44.5%)	
Capillary blood glucose level (mean; mmol/L)	50.6 (SD, 13.4)	10–69
Capillary blood glucose range:		
<2.2 mmol/L	42 (18.3%)	
2.2–3.9 mmol/L	187 (81.7%)	
Serum creatinine level (mean; mg/dL)	2.2 (SD, 2.1)	0.3–11.5
Blood urea nitrogen level (mean; mg/dL)	36.3 (SD, 24.9)	4–129
HbA_{1c} lab test:		
Ordered	109 (47.6%)	
Not ordered	120 (52.4%)	
HbA_{1c} results (*n*=109):		
<53 mmol/mol (7.0%)	50 (45.9%)	
53–63 mmol/mol (7.0–7.9%)	26 (23.9%)	
≥64 mmol/mol (8.0%)	33 (30.3%)	

SD=standard deviation.

Chi-squared tests revealed that a significantly greater proportion of people with blood glucose levels <2.2 mmol/L were located on the 5th Floor South, a medical unit, in comparison with other units (chi^2=11.4; df=5; *P*=0.04; *Table 2* and *Figure 1*).

While episodes of severe hypoglycaemia most commonly occurred during the 07.00 to 15.00 work shift, there was no significant difference in capillary blood glucose levels based on provider work shifts. Overall, 48.0% of participants had a blood glucose level <3.9 mmol/L between day 2 and 4 of their stay in the hospital (*Table 3*). Notably, as we were investigating hospital-acquired hypoglycaemia only, we chose not to analyse the first 24 hours in hospital, as blood glucose levels in that period were likely to be impacted by external variables.

Chi-squared tests show that there was a significantly higher percentage of patients with hypoglycaemia who had elevated BUN and serum creatinine levels (chi^2=100.0; df=1; *P*<0.001; *Table 4*). The relationships between BUN, serum creatinine and blood glucose levels were investigated using the Pearson product-moment correlation coefficient. There was a strong, positive correlation between BUN levels and serum creatinine levels (*r*=0.67; *P*=0.01). Given the age of the study population and the poor thirst mechanism present in many older people, this finding was not surprising. There was also a small, negative correlation between BUN levels and blood glucose levels (*r*=–0.13; *P*=0.05), indicating that higher BUN levels were associated with lower blood glucose levels (*Table 5*). Blood glucose levels were not significantly related to the total number of medications given to the patients prior to their hypoglycaemic episode (*Table 6*).

Discussion

The aim of this study was to identify the factors contributing to hypoglycaemia in older people with type 2 diabetes in an inner city hospital. We conclude that hypoglycaemia in this group was associated with the following factors: elevated BUN and serum creatinine levels, patient location within the hospital and the day of hospital stay.

The prevalence of hypoglycaemia in older adults aged ≥65 years is unknown. What is known is that age affects counter-regulatory responses to hypoglycaemia, thereby placing older people at increased risk of severe hypoglycaemia. The ACCORD (Action to Control Cardiovascular risk in Diabetes) trial demonstrated that adults aged ≥65 years had approximately a 50% increase in the rate of severe hypoglycaemia compared with middle-aged people (Miller et al, 2010). These data support the association of dementia with severe hypoglycaemia in older people (Kirkman et al, 2012).

Page points

1. Hypoglycaemia was associated with location within the hospital; in particular, severe hypoglycaemia was most common in 5th Floor South, a general medical ward.
2. Hypoglycaemia was also associated with the day of hospital stay: half of all episodes occurred between days 2 and 4.
3. Elevated blood urea nitrogen and serum creatinine level (markers of renal insufficiency) were also linked to hypoglycaemia. Half of the cohort had elevations in both of these markers.

Table 3. Number of hypoglycaemic episodes (capillary blood glucose <3.9 mmol/L) according to day of stay in hospital (*n*=229).

Day of stay	*n*
Day 2	27 (11.8%)
Day 3	41 (17.9%)
Day 4	42 (18.3%)
Day 5	19 (8.3%)
Day 6	17 (7.4%)
Day 7	14 (6.1%)
Day 8	13 (5.7%)
Day 9	6 (2.6%)
Day 10	9 (3.9%)
Day 11	4 (1.7%)
Day 12 or later	37 (16.2%)

Table 2. Rates and degree of hypoglycaemia by hospital unit.

Hospital floor	Hypoglycaemia severity*	*n*	Mean CBG (mmol/L)
4th Floor South	Severe	2	1.7
	Mild	31	3.1
4th Floor North	Severe	8	1.7
	Mild	40	3.1
5th Floor South	Severe	15	1.4
	Mild	30	3.1
5th Floor North	Severe	6	1.7
	Mild	41	3.1
6th Floor South	Severe	9	1.7
	Mild	34	3.1
6th Floor North	Severe	2	1.4
	Mild	11	3.1

*Severe defined as a CBG <2.2 mmol/L; mild defined as a CBG of 2.2–3.9 mmol/L.
CBG=capillary blood glucose; SD=standard deviation.

The largest subgroup in our study comprised 115 people (50.2%) who had elevated BUN in conjunction with elevated serum creatinine – and thus who likely had renal insufficiency. Even though glomerular filtration rate (GFR) has been shown to be a more reliable tool for indicating renal insufficiency (Moen et al, 2009), participants' GFR values were not available at the time of data collection. Thus, for the purpose of this study, renal insufficiency was evaluated using serum creatinine and BUN levels. Elevated BUN levels alone should not be viewed as a definitive cause of hypoglycaemia as they can be related to multiple other factors; however, the combination of elevated serum creatinine and elevated BUN have been identified as a risk factor for hypoglycaemia (Moen et al, 2009).

There was no glucose-lowering medication adjustment algorithm in place in this institution at the time of this study. The study was a retrospective chart analysis and involved a large number of prescribers with widely differing prescribing practices. Thus, there was no consistency in dose adjustments or decisions on which medication would be eliminated first in the event of hypoglycaemia.

Whereas one might expect that a larger number of antidiabetes medications would result in an increased rate of hypoglycaemia, surprisingly, there was no significant difference in capillary blood glucose levels based on the total number of medications given to the patients prior to their hypoglycaemic episodes (*Table 6*).

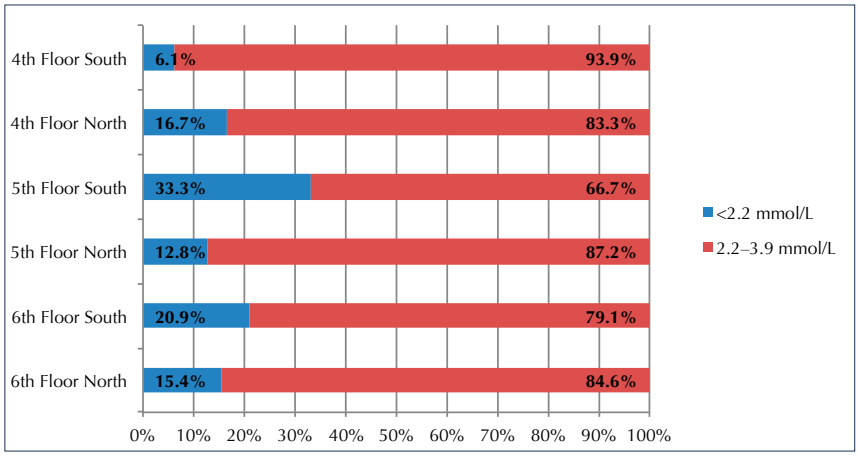

Figure 1. Proportion of hypoglycaemic episodes within hospital floors (n=229).

Limitations

This study is primarily limited by the fact that it was a retrospective chart review with hand-written medical records. Much of the desired information was simply unable to be obtained. The study was further limited by the inability to obtain GFR results. Instead, BUN and creatinine levels were used to assess renal status.

Another limitation is that we only collected information about glucose-lowering medicines. Other medications and polypharmacy can contribute to hypoglycaemia, as can many over-the-counter medications. However, the focus of this study was on the impacts of the antidiabetes medications primarily responsible for inducing hypoglycaemia, and so the decision was made not to review other medications.

This institution is located in Queens County, New York. Queens is one of the most ethnically and racially diverse counties in the US, and thus it is unknown whether findings from this study can be generalised to the various ethnicities that made up the cohort.

Table 4. Rates of normal and abnormal BUN and serum creatinine levels (*n*=229).

	Normal serum creatinine (≤1.3 mg/dL)	Elevated serum creatinine (>1.3 mg/dL)
Normal BUN (≤23 mg/dL)	74 patients (32.3%)	7 patients (3.1%)
Elevated BUN (>23 mg/dL)	33 patients (14.4%)	115 patients (50.2%)

BUN=blood urea nitrogen.

Table 5. Pearson product-moment correlations between test results (*n*=229).

	BUN	Serum creatinine
BUN	–	–
Serum creatinine	0.699*	–
Capillary blood glucose	–0.133†	–0.033

*Correlation is significant at the 0.01 level (2-tailed).
†Correlation is significant at the 0.05 level (2-tailed).
BUN=blood urea nitrogen.

Table 6. Number of mild and severe hypoglycaemic episodes according to total number of medications administered previously.

	Mild hypoglycaemia (CBG 2.2–3.9 mmol/L)	Severe hypoglycaemia (CBG <2.2 mmol/L)
No medication	16 (76.2%)	5 (23.8%)
1 medication	69 (77.5%)	20 (22.5%)
2 medications	90 (85.7%)	15 (14.3%)
≥3 medications	12 (85.7%)	2 (14.3%)

CBG=capillary blood glucose.

Finally, it would have been useful to examine whether a prespecified glucose-lowering medication adjustment algorithm would have reduced hypoglycaemia rates.

Conclusions and recommendations

The risk of hypoglycaemia remains a significant concern for older inpatients with diabetes (Braithwaite et al, 2004). Given that hospitalised older people are presumably better supervised than those living alone in their homes, this study further highlights concerns for the older population being treated with glucose-lowering agents.

With this knowledge, healthcare providers should consider proactive adjustment of diabetes medications for patients experiencing elevations in BUN and serum creatinine. Implementation of specific medication adjustment algorithms addressing the elimination of sulfonylurea use, lowering of basal and prandial insulin doses and/or changing to shorter-acting agents is recommended.

Nursing staff should also consider additional monitoring of capillary blood glucose values, specifically in the middle of the night, early in the morning shift and again prior to breakfast.

This study identified gaps that need to be evaluated in order to better understand precisely what is causing hypoglycaemia in older inpatients. These gaps include clarity of documentation on patients' prior history of type 2 diabetes, patient nutritional status, missing HbA_{1c} values and GFR results.

Hypoglycaemia continues to be the major limiting factor in the establishment of appropriate glycaemic control. Precise rates of hypoglycaemia in older people remain unknown. This study identified risk factors and patterns of hypoglycaemia in older inpatients with type 2 diabetes. Further research is needed to evaluate why most episodes occur in the first 3 days of the hospital stay, and why, and at exactly what time, they first occur during the morning shift. With more research, new practice guidelines can be developed to ensure patient safety, by reducing the rate of hypoglycaemia in this vulnerable population. ■

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Page points

1. The authors conclude that healthcare providers should consider proactive adjustment of diabetes medications for inpatients experiencing elevations in blood urea nitrogen and serum creatinine.
2. Nursing staff should also consider additional blood glucose monitoring in the middle of the night, early in the morning shift and again prior to breakfast.
3. Further research is needed to evaluate why most hypoglycaemic episodes occur in the first 3 days of the hospital stay and during the morning shift.

"With more research, new practice guidelines can be developed to ensure patient safety, by reducing the rate of hypoglycaemia in this vulnerable population."

Authors

Nataliya Shaforost is a faculty member at the College of Nursing at SUNY Downstate Medical Center, Brooklyn, New York, NY, USA; Donna Jornsay is Diabetes Nurse Educator at Long Island Jewish Medical Center, New Hyde Park, New York, NY, USA.

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