MEDINFO 2021: One World, One Health – Global Partnership for Digital Innovation
P. Otero et al. (Eds.)

doi:10.3233/SHTI220099

Recurrence of Hypoglycemia in Hospitalized Adult Patients in Non-Critical Areas: An Opportunity to Improve Patient Care Using Electronic Health Records

Lucía Llera[a], María Florencia Grande Ratti[b], Oscar Ignacio Jauregui[c], Carlos Martin Otero[c], Daniel R Luna[c], Mariana Burgos[b], María Paula Russo[a]

[a] *Department of Internal Medicine, Hospital Italiano de Buenos Aires, Argentina*
[b] *Internal Medicine Research Unit, Hospital Italiano de Buenos Aires, Argentina*
[c] *Departamento de Informática en Salud, Hospital Italiano de Buenos Aires, Argentina*

Abstract

Electronic Health Records offer an opportunity to improve patient care (in terms of quality and/or safety) by making available patient health information stored in a single Clinical Data Repository.

We aimed to estimate the frequency of hypoglycemic recurrences in hospitalized adult patients in non-critical areas. We designed a cross sectional study with hospitalizations between 2017 and 2018, which included patients with at least one hypoglycemia health record (defined as a value <70 mg/dL, either by capillary glycemic monitoring or serum measurement). Recurrence was defined as those who presented a second event, with at least 2 hours of difference.

We included 1884 patients, and 573 presented recurrences, yielding a global prevalence of 30.41% (95%CI 28.34-32.54). Due to the high frequency, it is important to identify vulnerable populations, to implement preventive measures to assist clinicians for decision-making tasks, as a clinical decision support system.

Keywords:

Electronic Health Records; Hypoglycemia; Recurrence.

Introduction

Hypoglycemia, defined as a value <70 mg/dL, is associated with an increased morbidity and mortality in hospitalized patients [1], and it's considered a poor prognostic marker in conditions such as sepsis, malnutrition, kidney or heart failure, acting as a significant barrier to optimal inpatient glycemic control [2].

There is an association between inpatient hypoglycemia and longer length of stay [3,4]. The NICE-SUGAR study showed 45% events of moderate hypoglycemia (defined as values between 41 and 70 mg/dL) and 3.7% events of severe hypoglycemia (≤41 mg/dL), both more frequent in the control group intensive [3].

A situation that may occur in the hospital setting is recurrence of hypoglycemia. Literature is limited in terms of describing frequency, associated factors, and most of the evidence exclusively includes patients from critical areas [5] and with diabetes [1].

A single Clinical Data Repository offers an opportunity to improve patient care, in terms of quality and/or safety, by making available patient health information, real-time monitoring and reporting systems. The establishment of an effective program could reduce errors in the recognition of hypoglycemia and consecutive treatment. That could be possible by using Electronic Health Records (EHR) and clinical decision support system (CDSS).

This study aimed to estimate the frequency of recurrence of hypoglycemia in adults hospitalized in non-critical areas with and without diabetes, and to explore associated factors.

Methods

Design and sample size

We designed a cross-sectional study which includes all consecutive hospitalized patients in non-critical areas, older than 18 years, between 1 January 2017 to 31 December 2018 in Hospital Italiano de Buenos Aires (HIBA), who had presented at least a blood glucose value lower than 70 mg/dL, either by historical records of capillary glycemic monitoring or serum measurement. We excluded pregnant women.

Setting

The HIBA is a third-level hospital from Argentina, with a capacity of 750 beds.

Data collection and information management

All health care information related to patients is stored in a single Clinical Data Repository (which has been in operation for more than 10 years and ensures the privacy and confidentiality of the data) to enable secondary analysis of the information. We used high-quality secondary administrative databases from EHR for retrospective data collection, by using all capillary glycemic monitoring or glycemia serum measurement (**Figure 1)**.

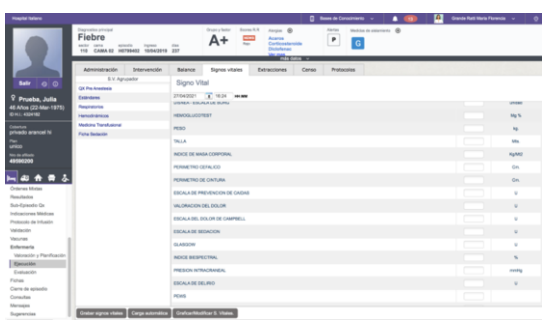


Figure 1 - EHR including capillary glycemic values

This study was approved by Institutional Review Board (#5118) and was conducted according to the amended declaration of Helsinki.

Statistical analysis

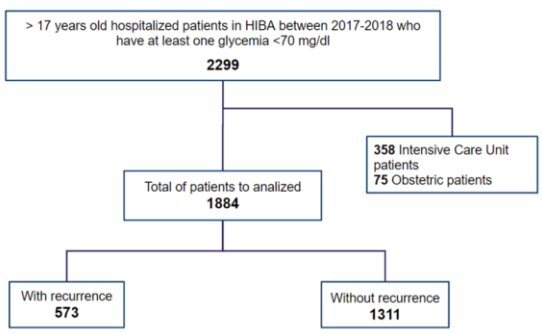
Regarding descriptive analysis, quantitative variables are presented according to the observed distribution as mean and standard deviation (SD), or median and interquartile range (IQR) or 25-75 percentiles. Categorical variables are presented as absolute frequency and relative frequency (percentage).

To identify associated factors with recurrence, we performed a logistic regression model, reporting the odds ratios (OR) and their respective 95%CI. We used STATA 16 software to perform statistical analysis.

Results

During the study period, we included 1884 patients with at least one episode of hypoglycemia for the analysis (**Figure 2**).

Figure 2 - flow diagram for study participants



Regarding baseline characteristics (**Table 1**): mean age of 65 years, 54% female and 23% previous diabetes (defined as an active problem registered in EHR).

A total of 573 patients presented recurrence of hypoglycemia, yielding a global prevalence of 30.41% (95%CI 28.34-32.54%).

Table 1 - Baseline characteristics

	All patients N = 1884	Recurrence group N = 573
Age, in years *	65.38 (19.54)	64.01 (18.49)
Female gender	54.30% (1023)	52.18% (299)
Diabetes	23.20% (437)	26.18% (150)
Cirrhosis	5.63% (106)	7.50% (43)
Bacteremia and/or Infection	16.45% (310)	21.99% (126)
Renal failure (clearance <60 ml/min/1,73m2)	47.98% (904)	56.37% (323)
Insulin	52.65% (992)	46.42% (266)
Insulin scheme		
basal only	14.65% (276)	19.37% (111)
bolus only	38.00% (716)	45.55% (261)
basal-bolus	13.32% (251)	18.50% (106)
Glucocorticoids	53.98% (1017)	61.95% (355)
Fast (at some point of hospitalization)	50.90% (959)	56.20% (322)
ICU requirements	48.94% (922)	56.89% (326)

* mean (standard deviation)

In-hospital mortality was 18.63% (351) and the median length of hospital stay was 10 days (percentiles 25-75: 6 and 21.5). While in the subgroup with recurrence, mortality was 24.61% (141) and the median time of hospital stay was 15 days (percentiles 25-75: 7 and 32).

Table 2, **Table 3** and **Table 4** show the prevalence stratified by sex, age group and diabetes respectively. When stratifying in ≥60 years of age, the prevalence was 29.26% (95%CI 26.74-31.87) and in those under 60 years it was 32.65% (95%CI 29.03-36.44). When stratifying in ≥80 years of age, the prevalence was 25.33% (95%CI 21.67-29.26) and in those under 80 years it was 32.39% (95%CI 29.91-34.96).

Table 2 - prevalence of recurrence stratified by sex

	N	Total	Prevalence	95%CI
Female	299	1023	29.22%	26.45-32.12
Male	274	861	31.82%	28.72-35.05

Table 3 - prevalence stratified by age group

Years	N	Total	Prevalence	95%CI
<20	8	18	44.44%	21.53-69.24
>=20 & <30	25	95	26.31%	17.80-36.35
>=30 & <40	40	136	29.41%	21.91-37.82
>=40 & <50	50	163	30.67%	23.70-38.36
>=50 & <60	86	228	37.71%	31.40-44.35
>=60 & <70	117	346	33.81%	28.84-39.06
>=70 & <80	113	369	30.62%	25.95-35.60
>=80 & <90	97	354	27.40%	22.81-32.36
>=90	37	175	21.14%	15.34-27.94

Table 4– prevalence stratified by previous diabetes

	N	Total	Prevalence	95%CI
With diabetes	423	1447	29.23%	26.89-31.65
Without diabetes	150	437	34.32%	29.87-38.98

The median global recurrence value of glycemia was 63 mg/dL. However, after stratification, it was 64 mg/dL in patients without diabetes and 60 mg/dL in patients with previous diabetes (p<0.01).

Regarding patients who recurred, they presented: mean 64 years, 52.18% female, 26.18% with a history of diabetes, 46.42% received insulin therapy, 56.20% fasted for some time during hospitalization, and 56.89% went through ICU.

Associated factors of recurrence (shown in **Table 5**) observed were: longer hospital stay (median of 15 days, compared to 9 days; OR 1.71; 95%CI 1.01-1.02) and in-hospital death (24.61% in compared with 16.02%; p <0.01). Additionally: diabetes (OR 1.26; 95%CI 1.01-1.59), renal failure (OR 1.62; 95%CI 1.33-1.97), cirrhosis (OR 1.60; 95%CI 1.07-2.39), infections (OR 1.72; 95%CI 1.34-2.22), insulin therapy (OR 1.52; 95%CI 1.24-1.86), glucocorticoids therapy (OR 1.59; 95%CI 1.30-1.95) and fast at some point of hospitalization (OR 1.35; 95%CI 1.11-1.65).

Table 5– associated factors with recurrence

	With recurrence (n: 1311)	Without recurrence (n: 573)	p value
Age*	65.98 (19.99)	64.00 (18.49)	**0.04**
Female	55.23% (724)	52.18% (299)	0.22
Diabetes	21.89% (287)	26.18% (150)	**0.04**
Renal failure	44.32% (581)	56.37% (250)	**0.01**
Cirrhosis	4.81% (63)	7.50% (43)	**0.02**
Infection	14.04% (184)	21.99% (126)	**0.01**
Insulin	36.23% (475)	46.42% (266)	**0.01**
basal	12.59% (165)	19.37% (111)	**0.01**
bolus	34.71% (455)	45.55% (261)	**0.01**
both	11.06% (145)	18.50% (106)	**0.01**
Corticosteroids	50.50% (662)	61.95% (355)	**0.01**
Fast	48.59% (637)	56.20 (322)	**0.01**
Length of stay (days) **	9 (5 - 18)	15 (7 - 32)	**0.01**
ICU	45.46% (596)	56.89% (326)	**0.01**
In-hospital mortality	16.02% (210)	24.61 (141)	**0.01**

* Means (Standard Deviation)
** Median and InterQuartile Range

Discussion

The recurrence of hypoglycemia was a frequent event in non-critically ill patients, with a global prevalence of 30%.

The main strength of our study was the existence of clinical data and personal health records integrated to the EHR as a key factor for viability. It was the resource of retrospective data collection necessary for the project. This single Clinical Data Repository helps to manage, collect, retrieve, process, store and distribute relevant information for the fundamental processes and the particularities of each organization, offering the opportunity to improve patient care (in terms of quality and/or safety) by making available patient information already stored.

Regarding limitations, we have to mention those related to the research design. It was a cross-sectional study, and it was not possible to establish the directionality of the associations. Additionally, other variables of interest could not be explored, such as the management after the first episode of hypoglycemia, the times to recurrence, or the causes of hypoglycemia (initial or recurrent).

Our finding (30% of recurrence of hypoglycemia in hospitalized adult patients) was lower compared with another study that reported a prevalence of 40% [6], but the other study was made on patients with a diagnosis of diabetes and insulin treatment, while 76% of patients in our population did not present with diabetes and only 52% were receiving insulin treatment. It is worthwhile to mention that the prevalence of diabetes in our study was higher than a previous local study [7]. This could be explained by different populations: the previous one included all hospitalizations, while this project was restricted only to those who had at least one episode of hypoglycemia in non-critical areas.

Regarding global mortality, was also higher compared to the previous local study (18% versus 10% respectively) probably because, in this case, it is a more complex population or with worse clinical conditions [7]. The risk of in-hospital mortality was higher in patients with recurrence of hypoglycemia, compared to those who did not (24% in the recurrence group and 16% in the non-recurrence group; $p<0.01$).

Consistent with literature review [8], we found that recurrence of hypoglycemia was associated with infections (OR 1.72). As we can observe in the NICE-SUGAR study [9], severe sepsis is an independent risk factor for hypoglycemia, and some authors suggest the use of hypoglycemia as a biomarker of severity.

Also, it is already known that a preventive practice could be the modification in treatment, such as the simple decrease in insulin dose, they are not implemented systematically. In a retrospective cohort conducted in 2016, the recommended 20% reduction in total daily insulin after the hypoglycemic event was only performed in 44% of patients [10].

Other factors associated with recurrence of hypoglycemia were: ICU requirements, length of stay and in hospital mortality, which mentions the impact on the prognosis of these patients.

Despite this, a small minority of hypoglycemia encountered in clinical practice is known to be spontaneous and therefore not induced by hypoglycemic agents [11]. These spontaneous hypoglycemic events confront the treating physician with a diagnostic conundrum. Although the autonomic and neuroglycopenic symptoms of hypoglycemia can be recognized by the trained clinician even in a patient who is not receiving insulin, it remains difficult to acknowledge the etiology of a spontaneous hypoglycemic event. Recent studies indicate that spontaneous rather than iatrogenic hypoglycemia is associated with a higher mortality rate, implying that hypoglycemia is just a biomarker and not a cause of death [12].

The results of our study represent very useful information for optimizing the evaluation of patients and the construction of preventive hospital management protocols [2]. Consistent with the literature, it is clear the need to improve the quality of clinical records and education of the health team to achieve greater diffusion and use of national and international therapeutic guidelines for the management of these patients [13,14].

This project was an example of data management based on EHR, interoperability and integration of informatics systems that make data quality. In the future, it will be necessary to provide an opportunity for the development of specific strategies aimed at preventing the recurrence of hypoglycemia in the most vulnerable people [15]; as well to reevaluate new management and prevention measures (such as CDSS), since despite having guidelines and protocols aimed at properly evaluating and treating hypoglycemia, the prevalence of recurrence is still high.

Conclusions

The global prevalence of hypoglycemic recurrences in hospitalized adult patients in non-critical areas was 30%. Due to the high frequency, it is important to identify vulnerable populations, to implement preventive measures to assist clinicians for decision-making tasks, as a clinical decision support system.

Acknowledgements

Dr DIEGO GIUNTA (Chief of Internal Medicine Research Unit) and Dr JAVIER POLLAN (Chief of Department of Internal Medicine) who provided general support.

References

[1] Rubin DJ, Golden SH. Hypoglycemia in non-critically ill, hospitalized patients with diabetes: evaluation, prevention, and management. Hosp Pract 2013 Feb;41(1):109–16. Available from: http://dx.doi.org/10.3810/hp.2013.02.1016

[2] Braithwaite SS, Buie MM, Thompson CL, Baldwin DF, Oertel MD, Robertson BA, et al. Hospital hypoglycemia: not only treatment but also prevention. Endocr Pract 2004 Mar;10 Suppl 2:89–99.

[3] NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SY-S, Blair D, Foster D, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med 2009 Mar 26;360(13):1283–97.

[4] Lake A, Arthur A, Byrne C, Davenport K, Yamamoto JM, Murphy HR. The effect of hypoglycaemia during hospital admission on health-related outcomes for people with diabetes: a systematic review and meta-analysis. Diabet Med 2019 Nov;36(11):1349–59. Available from: http://dx.doi.org/10.1111/dme.14115

[5] Turchin A, Matheny ME, Shubina M, Scanlon JV, Greenwood B, Pendergrass ML. Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. Diabetes Care 2009 Jul;32(7):1153–7. Available from: http://dx.doi.org/10.2337/dc08-2127

[6] Sorokin R, Varghese P, Gleason V, Senholzi C, Jabbour S, Gottlieb JE. Hypoglycemia in hospitalized patients treated with antihyperglycemic agents. J Hosp Med 2007 Jul 1;2(4). Available from:

https://cdn.mdedge.com/files/s3fs-public/pdfs/journals/212_ftp.pdf

[7] Russo MP, Grande Ratti MF, Giunta DH, Elizondo CM. Hospitalized patients with stress hyperglycemia: incidence of diabetes and mortality on follow-up. Endocrinol Diabetes Nutr 2018 Dec;65(10):571–6. Available from: http://dx.doi.org/10.1016/j.endinu.2018.07.005

[8] Brunkhorst FM, Engel C, Bloos F, Meier-Hellmann A, Ragaller M, Weiler N, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med 2008 Jan 10;358(2):125–39. Available from: http://dx.doi.org/10.1056/NEJMoa070716

[9] Bellomo R, Egi M. Hypoglycemia in sepsis: biomarker, mediator, or both? Crit Care Med 2011 Oct;39(10):2367–9. Available from: http://dx.doi.org/10.1097/CCM.0b013e31822a5be5

[10] Mathioudakis N, Everett E, Golden SH. PREVENTION AND MANAGEMENT OF INSULIN-ASSOCIATED HYPOGLYCEMIA IN HOSPITALIZED PATIENTS. Endocr Pract 2016 Aug;22(8):959–69. Available from: http://dx.doi.org/10.4158/EP151119.OR

[11] Martens P, Tits J. Approach to the patient with spontaneous hypoglycemia. Eur J Intern Med 2014 Jun;25(5):415–21. Available from: http://dx.doi.org/10.1016/j.ejim.2014.02.011

[12] Hulkower RD, Pollack RM, Zonszein J. Understanding hypoglycemia in hospitalized patients. Diabetes Manag 2014 Mar;4(2):165–76.

[13] Griffing KL. Hypoglycemia Prevention in Hospital Patients: A Quality Improvement Project to Prevent Severe and Recurrent Hypoglycemia. Clin Diabetes 2016 Oct;34(4):193–9. Available from: http://dx.doi.org/10.2337/cd15-0055

[14] American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care 2013 Apr;36(4):1033–46. Available from: http://dx.doi.org/10.2337/dc12-2625

[15] D'Netto M, Murphy CV, Mitchell A, Dungan K. Predictors of recurrent hypoglycemia following a severe hypoglycemic event among hospitalized patients. Hosp Pract 2016;44(1):1–8. Available from: http://dx.doi.org/10.1080/21548331.2016.1130584

Address for correspondence

María Florencia Grande Ratti

Mail: maria.grande@hospitalitaliano.org.ar

Address: Juan D. Perón 4190 (C1181ACH)

Buenos Aires, Argentina.