

# HYPOGLYCEMIA IN EMERGENCIES : FACTORS PREDICTING HOSPITALIZATION A MULTIVARIATE ANALYSIS OF 43 CASES

## HYPOGLYCEMIE AUX URGENCES : FACTEURS PREDICTIFS D'HOSPITALISATION UNE ANALYSE MULTIVARIÉE DE 43 CAS

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### Abstract

**Purpose:** The aim of the study was to describe epidemiological features of the patients who consult emergencies for hypoglycemia and to identify the predictive factors of hospitalization

**Materials and methods:** Transversal study over a period of 18 months. We have included all emergency consultants for clinical-biological hypoglycemia. Two groups of patients were compared: Those who were hospitalized (H+ group) and those who were not hospitalized (H- group)

**Results:** We identified 43 cases of hypoglycemia. The majority of our patients were diabetics (93%). Capillary blood glucose averaged  $0.4 \pm 0.11$  g/l. Hospitalization was indicated in 19 patients (44%). The independent predictive factors of hospitalization were : history of hypoglycemia , hypoglycemia at home , chronic renal failure, creatinine level  $\geq 200$   $\mu\text{mol/l}$ , hypoglycemic coma and seizures.

**Conclusion:** All of these results highlight the important percentage of potentially avoidable hospitalizations.

**Key - words:** Hypoglycemia ; Emergencie ; Predictive factors et Hospitalization

### Résumé

**Objectif :** Le but de l'étude était de décrire les caractéristiques épidémiologiques des patients consultant en urgence pour hypoglycémie et d'identifier les facteurs prédictifs d'hospitalisation

**Méthodologie :** Une étude transversale s'est déroulée sur une période de 18 mois en incluant tous les consultants en urgence pour hypoglycémie clinico-biologique. Deux groupes de patients ont été comparés : ceux qui ont été hospitalisés (groupe H+) et ceux qui n'ont pas été hospitalisés (groupe H-).

**Résultats :** Nous avons identifié 43 cas d'hypoglycémie. La majorité de nos patients étaient diabétiques (93%). La glycémie capillaire était en moyenne de  $0,4 \pm 0,11$  g/l. L'hospitalisation a été indiquée chez 19 patients (44%). Les facteurs prédictifs indépendants d'hospitalisation étaient : l'antécédent d'hypoglycémie, hypoglycémie à domicile, insuffisance rénale chronique, taux de créatinine  $\geq 200$   $\mu\text{mol / l}$ , le coma hypoglycémique et les convulsions.

**Conclusion :** L'ensemble de ces résultats met en évidence le nombre important d'hospitalisations potentiellement évitables.

**Mots – clés :** Hypoglycémie ; Urgence ; Facteurs prédictifs ; Hospitalisation

### ملخص

**الهدف:** وصف الخصائص الوبائية للمرضى الذين يستشيرون قسم الطوارئ من أجل نقص السكر في الدم وتحديد العوامل التنبؤية للاستشفاء.

**المواد والأساليب:** دراسة على مدى 18 شهرًا. قمنا باحتساب جميع مرضى قسم الطوارئ لنقص سكر في الدم السريري و البيولوجي. تمت مقارنة مجموعتين من المرضى: أولئك الذين تم نقلهم إلى المستشفى (مجموعة +) وأولئك الذين لم يتم النتائج: حددنا 43 حالة من حالات نقص سكر الدم. غالبية مرضانا مصابون بمرض إدخالهم إلى المستشفى (مجموعة -) السكر (93%). كان متوسط نسبة السكر في الدم الشعري  $0.4 \pm 0.11$  جم / لتر .

**المؤشرات المستقلة للدخول إلى المستشفى:** تاريخ نقص السكر في الدم ، نقص السكر في الدم في المنزل، الفشل الكلوي المزمن، مستوى الكرياتينين  $\leq 200$  ميكرو لتر / لتر ، غيبوبة سكر الدم ، النوبات على التوالي الخلاصة: تسلط كل هذه النتائج الضوء على العدد الكبير من حالات الاستشفاء التي يمكن تجنبها

**الكلمات المفتاحية:** نقص السكر في الدم ; الطوارئ ; العوامل التنبؤية ; الاستشفاء.

## INTRODUCTION

Hypoglycemia is the most common metabolic complication of diabetes. It is less common in non-diabetics.

Numerous studies have highlighted the dangers and side effects of intensified diabetes treatments. Hypoglycemia is a dramatic, predictable and preventable consequence of treatment for the diabetic patient.

It can lead to emergency room consultation even to hospitalization, with a significant financial cost and possible consequences in terms of morbidity and mortality.

We proposed, in this work, to describe the epidemiological and clinical characteristics of patients who consult emergencies for hypoglycemia and to seek the predictive factors of hospitalization.

## PATIENTS AND METHODS

Our study was transversal, conducted in the emergency department of the regional hospital of Mahres.

It was conducted over a period of 18 months (01/01/2015 - 30/06/2016).

We included emergency room consultants for clinical-biological hypoglycemia (capillary blood glucose  $\leq 0.5$  g/l in the non-diabetic and  $\leq 0.7$  g/l in the diabetic).

We excluded patients already treated in the basic health care centers and those with lacking clinical or biological data.

For each patient, we collected those parameters:

- Demographic: age, gender and medical-history.
- Nosological: place of occurrence and triggering factor.
- Clinical: systolic blood pressure, diastolic blood pressure, heart rate, respiratory frequency, pulsed saturation of oxygen (SpO<sub>2</sub>), Glasgow Coma Scale (GCS) [1], neurovegetative signs (pallor, sweating, nausea, vomiting ...) and neuroglycopenic signs of hypoglycemia (coma state (GCS  $\leq 12$ ), tremor, confusion, concentration problems, slurred speech ...)
- Biological: Capillary glucose level (before and after glucose administration), blood ionogram, blood glucose level, kidney function, liver function, blood count and hemostasis parameters.

- The initial severity was assessed by the Clinical Classification of Patients with Emergencies [2]
- Therapeutic: oral or intravenous glucose administration.

The statistical analysis included descriptive and analytic steps.

In the descriptive section, we calculated frequencies for the qualitative variables and means  $\pm$  standard deviation for the quantitative variables. In the analytical section, two groups of patients were compared: those who were hospitalized (H+ group) and those who were not hospitalized (H-group).

The qualitative variables were compared using the Chi<sup>2</sup> test or the exact Fischer test (when the theoretical size for a given group is less than 5). Quantitative variables were compared using the Student's t-test or the U-test according to the normality of the distribution.

Variables identified in univariate analysis were integrated into a binary logistic regression model to identify independent predictors of hospitalization. Thus, we calculated Odds ratios with a 95% confidence interval.

A  $p < 0.05$  was considered significant for all tests used.

## RESULTS

### Characteristics of patients

During the study period, 45634 patients consulted the emergency room of the regional hospital in Mahres.

Among these patients, there were 43 cases of hypoglycemia (0.09 %) (Figure 1).

The average age was  $56 \pm 20$  years with extremes ranging from 8 to 84 years. A male predominance was detected with a sex ratio of 1.7.

Forty-two patients (97.6%) had one or more medical history.

They were diabetic in 93% of the cases.

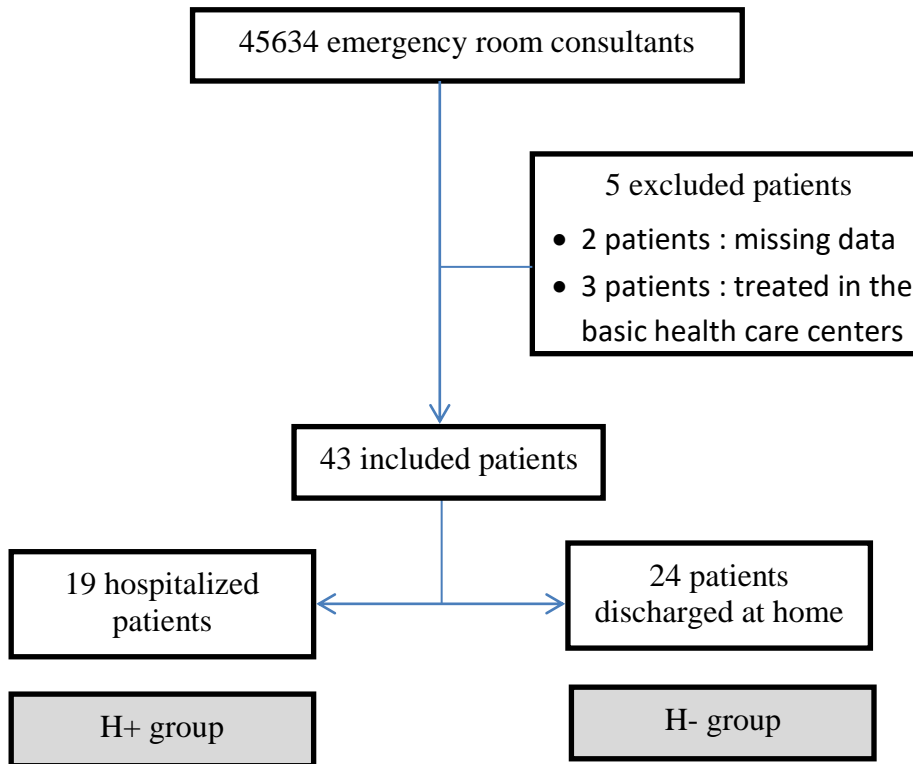
This is a diabetes associated with others defects (arterial hypertension, coronary artery disease, chronic renal failure and / or chronic respiratory failure) in 47.5% of cases.

The triggering factors were the scheme gap in 48.8% of the cases, an error of the insulin doses in 39.5% of the cases, a physical exercise in 23.2%

of the cases, an error of the doses of sulfamide in 13.9% of the cases and a sepsis in a diabetic in 13.9% of the cases.

The capillary glucose level was at  $0.4 \pm 0.11$  g/l with extremes ranging from 0.2 to 0.6 g/l. After intravenous or oral glucose administration, it averaged  $2.14 \pm 0.56$  g /l with extremes ranging from 1.1 to 3.1 g /l.

Most patients (86%) were in class 3 of the clinical classification of patients in emergencies. An immediate awakening was obtained in 90.7% of the cases. It was complete in 27 patients (62.8%) and partial in 12 patients (27.9%). The immediate evolution was favorable in 65.1% of the cases. It was enlarded with complications in 15 patients (34.9%) (Table 1).



**Figure 1:** The study flow chart.

**Table 1:** Complications post glucose administration

<b>Immediate complications</b>	<b>Number</b>	<b>Fréquence (%)</b>
<b>Hypoglycemic coma</b>	3	6.9
<b>Seizures</b>	2	4.6
<b>Paresis</b>	1	2.3
<b>High blood pressure</b>	11	25.5
<b>Acute pulmonary edema</b>	1	2.3

***Factors predictive of hospitalization***

After a temporary improvement, 56% of patients were discharged at home. Five patients (12%) required hospitalization in the intensive care unit. Fourteen patients (32%) were hospitalized in the department of Medicine.

Comparing the two groups (H+group and H-group), patients in H + group were significantly older. Type 1 diabetes, history of hypoglycemia, coronary artery disease or chronic renal failure were similarly significantly more frequent among hospitalized patients (Table 2).

The study of nosological parameters is summarized in (Table 3). The analysis of clinical parameters at admission showed that among the adrenergic signs, pallor and palpitation were significantly more frequent in hospitalized patients. Among the neuroglycopenic signs, coma status, difficulties of concentration and slurred speech were significantly more common in H+ group.

The Glasgow coma score was lower among hospitalized patients with no significant difference between the two groups (Table 4).

The analysis of biological parameters at admission showed that hospitalized patients had natremia and serum creatinine levels significantly higher compared to non-hospitalized patients (Table 5). Among the complications occurring during management at the emergency department, hypoglycemic coma, seizures, motor deficit and acute pulmonary edema were significantly more frequent in H+ group (Table 6).

In multivariate analysis, the following parameters were identified as independent predictors of hospitalization: history of hypoglycemia, chronic renal failure, home hypoglycemia, creatinine level  $\geq 200 \mu\text{mol/l}$ , hypoglycemic coma and seizures (Table 7).

**Table 2 : Demographic parameters**

	<b>H+ Group (n =19)</b>	<b>H- Group (n =24)</b>	<b>P</b>
<b>Age (years <math>\pm</math> SD)</b>	64.8 $\pm$ 12.6	52.7 $\pm$ 27.1	0
<b>Sex (Male / Female)</b>	2.1	1.4	0.13
<b>Diabetes type1 (N(%))</b>	14 (73.6)	14 (58.3)	0.04
<b>Diabetes type 2 (N(%))</b>	4 (26.3)	7 (29.1)	0.14
<b>History of hypoglycemia (N(%))</b>	12 (63.1)	5 (20.8)	0.01
<b>Age of diabetes (years <math>\pm</math> SD)</b>	17.3 $\pm$ 10.2	16.8 $\pm$ 9.5	0.6
<b>High blood pressure (N(%))</b>	7 (36.8)	13 (54.1)	0.68
<b>Coronary artery disease (N(%))</b>	5 (26.3)	3 (12.5)	0.02
<b>Chronic renal failure (N(%))</b>	3 (15.7)	0	0

**Table 3: Nosological parameters**

	<b>H+ Group (n =19)</b>	<b>H- Groupe (n =24)</b>	<b>P</b>
<b>At home hypoglycemia (N(%))</b>	16 (84.2)	18 (75)	0.03
<b>Hypoglycemia at work (N(%))</b>	1 (5.2)	2 (8.3)	0.1
<b>Hypoglycemia at a public place (N(%))</b>	2 (10.5)	2 (8.3)	0.06
<b>Hypoglycemia at a public road (N(%))</b>	1 (5.2)	1 (4.1)	0.1
<b>Scheme gap (N(%))</b>	10 (52.6)	11 (45.8)	0.02
<b>Physical exercise (N(%))</b>	4 (21)	6 (25)	0.1
<b>Insulin dose error (N(%))</b>	8 (42.1)	9 (37.5)	0
<b>Error in sulfamide doses (N(%))</b>	1 (5.2)	5 (20.8)	0.16
<b>Sepsis (N(%))</b>	5 (26.3)	1 (4.1)	0.04

**Table 4:** Clinical parameters at admission

	<b>H+ Group (n =19)</b>	<b>H- Groupe (n =24)</b>	<b>P</b>
<b>Systolic arterial pressure (mmHg <math>\pm</math> SD)</b>	122.4 $\pm$ 25.3	134.8 $\pm$ 19	0.07
<b>Diastolic arterial pressure (mmHg <math>\pm</math> SD)</b>	75.7 $\pm$ 12.8	76.8 $\pm$ 10.7	0.5
<b>Pulse rate (beats/min <math>\pm</math> SD)</b>	88 $\pm$ 10.5	86.5 $\pm$ 17.5	0.07
<b>Respiratory frequency (cyc/min <math>\pm</math> SD)</b>	16.5 $\pm$ 3.2	16.1 $\pm$ 2.1	0.2
<b>Pulsed saturation of oxygen (% <math>\pm</math> SD)</b>	95.8 $\pm$ 1.8	95.7 $\pm$ 1.9	0.7
<b>Pallor (N(%))</b>	12 (63.1)	15 (62.5)	0
<b>Sweating (N(%))</b>	10 (52.6)	15 (62.5)	0.1
<b>Nausea / vomiting (N(%))</b>	3 (15.7)	6 (25)	0.13
<b>Palpitation (N(%))</b>	4 (21)	4 (16.6)	0
<b>GCS (points <math>\pm</math> SD)</b>	9 $\pm$ 1.8	10 $\pm$ 2.4	0.8
<b>Coma (N(%))</b>	16 (84.2)	16 (66.6)	0.02
<b>Tremor (N(%))</b>	9 (47.3)	8 (33.3)	0.3
<b>Confusion (N(%))</b>	5 (26.3)	10 (41.6)	0.5
<b>Difficulties of concentration (N(%))</b>	2 (10.5)	2 (8.3)	0
<b>Slurred speech (N(%))</b>	8 (42.1)	3 (12.5)	0.03
<b>Drowsiness (N(%))</b>	3 (15.7)	4 (16.6)	0.3
<b>Sign of Babinski (N(%))</b>	5 (26.3)	4 (16.6)	0.15

**Table 5:** Biological parameters at admission

	<b>H+ Group (n =19)</b>	<b>H- Groupe (n =24)</b>	<b>P</b>
<b>Capillary blood glucose (g/l <math>\pm</math> SD)</b>	0.39 $\pm$ 0.1	0.40 $\pm$ 0.12	0.9
<b>Capillary blood glucose after resucrage (g/l <math>\pm</math> SD)</b>	2.12 $\pm$ 0.64	2.15 $\pm$ 0.49	0.06
<b>Glycemia (mmol/l <math>\pm</math> SD)</b>	10.8 $\pm$ 2.2	11.2 $\pm$ 1.6	0.07
<b>Natremia (mmol/l <math>\pm</math> SD)</b>	143 $\pm$ 4.1	139 $\pm$ 1.6	0.03
<b>Kaliemia (mmol/l <math>\pm</math> SD)</b>	4.3 $\pm$ 0.6	4 $\pm$ 0.4	0.1
<b>Urea (mmol/l <math>\pm</math> SD)</b>	8.6 $\pm$ 2.6	6.2 $\pm$ 0.7	0.06
<b>Creatinine (<math>\mu</math>mol/l <math>\pm</math> SD)</b>	112.3 $\pm$ 30.6	65 $\pm$ 22.6	0.01
<b>SGOT (IU/l <math>\pm</math> SD)</b>	38 $\pm$ 12.4	35 $\pm$ 7.2	0.7
<b>SGPT (IU/l <math>\pm</math> SD)</b>	34 $\pm$ 13.6	35 $\pm$ 6.4	0.6

SGOT : Serum Glutamyl Oxaloacetate Transferase

SGPT : Serum Pyruvate Oxaloacetate Transferase

**Table 6:** Immediate complications in univariate analysis

<b>Immediate complications</b>	<b>H+ Group (n =19)</b>	<b>H- Groupe (n =24)</b>	<b>P</b>
<b>Hypoglycemic coma (N(%))</b>	3 (15.7)	(0)	0
<b>Convulsion (N(%))</b>	2 (10.5)	(0)	0.001
<b>Paresis (N(%))</b>	1 (5.2)	(0)	0.01
<b>High blood pressure (N(%))</b>	7 (36.8)	4 (16.6)	0.12
<b>Acute pulmonary edema (N(%))</b>	1 (5.2)	(0)	0.01

**Table 7:** Independent predictors of hospitalization

Factors	P	OR	IC 95%	
			Min	Max
Diabetes type1	0.062	1.1	1.1	5.3
History of hypoglycemia	0.031	3.3	2.6	6.7
Coronary artery disease	0.4	1.7	1.1	3.5
Chronic renal failure	0.01	3.1	1.7	8.5
At home hypoglycemia	0.043	1.2	1.2	4.2
Scheme gap	0.146	1.2	0.9	1.7
Insulin dose error	0.436	1.3	1.2	2.8
Sepsis	0.893	1.6	0.9	3.1
Pallor	0.077	1.9	1.3	5.7
Palpitation	0.639	1.3	0.7	2.7
Difficulties of concentration	0.087	1.8	1.4	4.2
Slurred speech	0.429	1.1	1.1	2.8
Creatinine $\geq 200 \mu\text{mol/l}$	0.012	2.8	1.6	2.9
Hypoglycemic coma	0.001	2.5	2.1	7.9
Seizures	0.004	3.7	1.7	5.4
Paresis	0.247	1.2	0.9	1.9
Acute pulmonary edema	0.509	1.5	1.2	2.7

## DISCUSSION

In our study, the incidence of hospitalization following severe hypoglycemia was 44%. We identified as independent predictors of hospitalization: history of hypoglycemia, at home hypoglycemia, chronic renal failure, creatinine level  $\geq 200 \mu\text{mol/l}$ , hypoglycemic coma and seizures. The incidence of hospitalization is close to those described in previous studies. Budnitz DS et al [3] reported, in a population of 5077 patients aged 65 and over, 57.5% of emergency room consultations for severe iatrogenic hypoglycemia led to hospitalizations. In the United States of America, a one-year retrospective analysis of three emergency departments found that 41% of patients admitted to the emergency department for hypoglycemia were hospitalized. The independent predictors of hospitalization in this study were high age (over 65 and in particular over 75), treatment with hypoglycemic sulfamides, the absence of known antidiabetic treatment and the repetition of hypoglycemia in pre-hospital or in emergency (more than 3) [4]. A work carried out in the

urgencies of Toulouse university hospital concluded that type 1 diabetics are significantly more hospitalized when they are polymedicated, their last glycated hemoglobin is higher ( $\geq 7.5\%$ ), a diabetological opinion was taken in the emergency room and when the duration of emergencies is longer. Type 2 diabetics are significantly more hospitalized when they are over 75 years old, they have renal insufficiency and when hypoglycemia has occurred at home [5].

For most studies, the factors predicting hospitalization reflect the frailty of the patient: age, kidney failure, the existence of other pathology causing hypoglycemia (sepsis, liver disease, cancer) ... [6].

In our study, at home hypoglycemia appears as a predictor of hospitalization. In fact, patients who have hypoglycemia outside their home (on public roads or in the workplace) are active patients, and therefore often younger and in good health. An error in sulfamides doses is without significant difference between the two groups. In other studies, it is often associated with hospitalization [4, 7].

When we are interested in these patients under sulfamides not hospitalized, none returned to the emergency room for hypoglycemia. So it seems that advice given at the exit (decrease doses, intensify glycemic monitoring) were enough to avoid a new severe episode. Hypoglycemic coma and seizures also appear as predictors of hospitalization in our study. The relationship between hypoglycemia and disorders of higher functions is nevertheless difficult to evaluate because it is biased by diabetes itself, its seniority and its degenerative complications [8]. The neurological impact of severe hypoglycemia is dependent on the characteristics of hypoglycemia (duration, severity) and those of the patients (field, age, etc.) [9, 10]. Preliminary studies have allowed us to observe in rats with severe hypoglycemia neuronal necrosis lesions, mainly in the region of the hippocampus, which is responsible for memorization functions. Cerebral preconditioning, or adaptive response to glucose deprivation, has also been noticed in rats with moderate and repeated hypoglycemia, providing some protection against the consequences of severe hypoglycemia [11]. Regarding clinical studies, the influence of hypoglycemia on cognitive function seems less obvious. Indeed, in the cohort of DCCT, no association has been found between the frequency of severe hypoglycemia and the degradation of cognitive functions regardless of the initial randomization group [10]. However, impaired cognitive function increases the risk of severe hypoglycemia in diabetic patients, creating a real vicious circle [9].

Depending on the country and its different healthcare systems, the place of hypoglycemia in the economic context is difficult to quantify.

In France, a study was conducted to evaluate the annual number of hypoglycemia seen by private physicians as well as that of hospitalized hypoglycemia and to estimate the annual financial impact of these hospitalizations for the community [12]. There were 40.000 hypoglycemias, of which 10.800 led to hospitalization. At the time, the average cost of hospitalizations for hypoglycemia was estimated at 14.000 FF (2979.42 euros) for an average stay of 6.6 days, which, compared to the national population of the time, generates a cost of 108 to 151 million FF (23 to 32 million euros). This is in favor of the major number of potentially avoidable hospitalizations and the high costs of repeated hospitalizations related to hypoglycemia, and thus underline the interest of appropriate therapeutic management. During this work, we

have chosen to describe the patients who consult Mahres emergencies for hypoglycemia, as well as to identify the factors predicting hospitalization, which is rarely reported in the literature.

Some limits should be mentioned. Despite the transversal nature of our study and detailed information previously conducted among physicians in the emergency department, some data was collected from the medical records of the medicine department.

## CONCLUSION

All of these results highlight the major number of potentially preventable hospitalizations. Each prescription renewal should be accompanied by a therapeutic reassessment and education for both the diabetic and her family. Many emergency room visits could be avoided. Further studies are required to confirm our findings.

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