Rev. Fac. Med. Hum. 2024; 24(2):55-62.
DOI: 10.25176/RFMH.v24i2.6176
ORIGINAL PAPER

ISSN Versión Online: 2308-0531
Facultad de Medicina Humana URP
RFMH

# CASE-CONTROL STUDY ON FACTORS ASSOCIATED WITH HYPERGLYCEMIC CRISES IN DIABETIC ADULTS ATTENDED IN THE EMERGENCY UNIT OF A GENERAL HOSPITAL IN LIMA

## ESTUDIO DE CASOS Y CONTROLES SOBRE FACTORES ASOCIADOS A CRISIS HIPERGLUCÉMICAS EN ADULTOS DIABÉTICOS ATENDIDOS EN LA UNIDAD DE EMERGENCIA DE UN HOSPITAL GENERAL DE LIMA

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## ABSTRACT

**Introduction:** Diabetes mellitus represents a significant public health challenge; hyperglycemic crises are serious complications that can result in morbidity or death. Objective: To establish factors associated with hyperglycemic crises (HC) in diabetic adults attended in a hospital in Lima. **Methods:** An observational, retrospective, and analytical case-control study was conducted in a General Hospital in Lima between 2015 and 2019. A total of 186 medical records (62 cases and 124 controls) were selected through simple random sampling. The outcome was HC, defined as diabetic ketoacidosis, hyperosmolar hyperglycemic state, and mixed state. The variables included age, sex, area of residence, health insurance, duration of disease, comorbidities, acute infections, and medication adherence. Data were analyzed using Chi-Square tests and Fisher's exact test, calculating crude (cOR) and adjusted (aOR) Odds Ratios. **Results:** In the bivariate analysis, factors associated with HC were sex (p=0.029), age (p<0.001), duration of disease (p=0.001), and medication adherence (p<0.001). No relationship was found with variables such as residence, health insurance, acute infectious processes, and comorbidities (p>0.05). In the multivariate analysis, factors associated with HC were age (aOR: 2.85; 95% CI: 1.41–5.79; p=0.004) and non-adherence to medication (aOR: 3.87; 95% CI: 1.84–8.18; p<0.001). **Conclusion:** Factors associated with HC are age and non-adherence to medication.

**Keywords:** Diabetes mellitus; Hyperglycemia; Diabetic ketoacidosis; Diabetes complications. (Source: MESH-NLM)

## RESUMEN

**Introducción:** La diabetes mellitus representa un desafío significativo para la salud pública; las crisis hiperglucémicas son complicaciones serias que pueden resultar en morbilidad o muerte. **Objetivo:** Establecer factores asociados a las crisis hiperglucémicas (CH) en adultos diabéticos atendidos en un hospital de Lima. **Métodos:** Se realizó un estudio observacional, retrospectivo y analítico de casos y controles en un Hospital General de Lima entre 2015 y 2019. Se seleccionaron 186 historias clínicas (62 casos y 124 controles) mediante muestreo aleatorio simple. El desenlace fueron las CH, definidas como cetoacidosis diabética, el estado hiperosmolar hiperglucémico y el estado mixto. Las variables incluyeron edad, sexo, zona de residencia, seguro de salud, tiempo de enfermedad, comorbilidades, infecciones agudas y adherencia a la medicación. Los datos se analizaron con pruebas de Chi Cuadrado y la prueba exacta de Fisher, calculando Odds Ratios crudos (ORc) y ajustados (Ora). **Resultados:** En el análisis bivariado los factores que se asociaron con las CH fueron; el sexo (p=0,029), edad (p<0,001), tiempo de enfermedad (p=0,001) y adherencia a la medicación (p<0,001). No se halló relación con las variables residencia, seguro de salud, procesos infecciosos agudos y comorbilidades (p>0,05). En el análisis multivariado los factores asociados a las CH fueron la edad (ORa: 2,85; IC95%: 1,41–5,79; p=0,004) y la no adherencia a la medicación (ORa: 3,87; IC95%: 1,84–8,18; p<0,001). **Conclusión:** Los factores asociados a las CH son la edad y la no adherencia a la medicación.

**Palabras clave:** Diabetes mellitus; Hiperglucemia; Cetoacidosis diabética; Complicaciones de la diabetes (Fuente: DeCS- BIREME)

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Cite as: Lopez Bautista M, Córdova Sotomayor DA. Case-Control Study on Factors Associated with Hyperglycemic Crises in Diabetic Adults Attended in the Emergency Unit of a General Hospital in Lima. Rev Fac Med Hum. 2024;24(2):55-62. doi 10.25176/RFMH.v24i2.6176

Journal home page: http://revistas.urp.edu.pe/index.php/RFMH

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## INTRODUCTION

The World Health Organization (WHO) estimates that around 422 million people worldwide suffer from diabetes mellitus (DM), with more than sixty million cases in Latin America. Moreover, it is estimated that over 50% of these cases are not well controlled. It is important to highlight that the lack of control of this disease significantly increases the risk of severe complications and premature mortality. Hyperglycemic crises (HC) are the most severe acute metabolic complications of diabetes, which may require attention in a specialized care unit. Among the main HC observed in emergency units are diabetic ketoacidosis (DKA), hyperosmolar hyperglycemic state (HHS), and mixed state (MS)[1-4].

The factors associated with HC in adults with diabetes include a variety of elements that vary according to regional and clinical context, but there are common factors identified globally. In a study conducted in hospitals in Mexico, it was found that infections were the main cause of HC, representing 43% of the cases, followed by acute alcohol consumption, responsible for 22.6% of the cases [5]. Another study conducted in Ecuador during the COVID-19 pandemic showed that DKA and HHS can be triggered by SARS-CoV-2 infection, with fatal outcomes in some cases of DKA[6]. Additionally, irregular adherence to antidiabetic treatment has also been identified as a significant risk factor for these complications[7]. These studies highlight the importance of adequate management of treatment and infection control to prevent these potentially fatal crises.

Despite these findings, there are unexplored areas regarding the specific risk factors for HC in different geographical and population contexts. In particular, in Lima, Peru, no recent studies have comprehensively addressed this problem in general hospital emergency services. This is crucial due to the high incidence of diabetic decompensations in the region, which represents a significant threat to patient health and a high economic cost for the healthcare system. Given this scenario, the objective of this research is to establish the factors associated with HC in diabetic patients treated in the emergency unit of a general hospital in Lima over a five-year period.

## METHODS

### Design and Study Area

The study was observational, retrospective, and analytical, of the case-control type. The research was conducted in the emergency service of a General Hospital in Lima, covering a period of five years, from 2015 to 2019.

### Population and Sample

The research was based on a population of 3,580 patients treated in the emergency service of a General Hospital in Lima over a five-year period from 2015 to 2019. The sample size was determined using the specific formula for case-control studies, with a 95% confidence level, 80% power, and expected proportions of exposed age of 16.5% and 37.1% from a previous study[8]; resulting in a sample of 186 medical records of patients with diabetes. Of these, 62 were those who developed an HC (cases), and 124 were those who did not present such crises (controls). Simple random sampling was applied. The selection criteria included the readability of all medical records and the presence of complete data in patients diagnosed with type 1 and type 2 diabetes mellitus.

### Variables and Instruments

The dependent variable was the presence of HC, which was defined as the occurrence of HC, including DKA, HHS, and MS. The independent variables were gender (male or female), age (under 60 years or 60 years and older), area of residence (urban or rural), health insurance (with or without coverage), duration of illness (less than 10 years or 10 years or more), comorbidities (diseases in addition to diabetes), acute infectious processes (infections during admission), and medication adherence (consistency in following the treatment, with or without adherence). A registration form designed for this study was used to collect the data, documenting variables from the medical records, including sociodemographic data, pathological history, details about the HC, and treatment adherence.

### Procedure

The study was approved by the corresponding entities, and the medical records of patients who met the selection criteria were requested from the archives department. Simple random sampling was used to select 186 medical records out of a total of 3,580, of which 62 were of patients with HC (cases) and 124 without crises (controls). The information was collected in a data collection form specifically designed for the study. The data obtained were analyzed and presented as percentages through frequency distribution tables.

### Statistical Analysis

For the bivariate study, the Chi-Square test and Fisher's exact test were used when the expected frequencies were greater than five and less than or equal to five, respectively. The crude Odds Ratio (ORc) and adjusted Odds Ratio (ORa) were calculated, with 95% confidence intervals and a significance level of $p < 0.05$. SPSS version 22 statistical software was used to perform this analysis.

### Ethical Aspects

This study respected the confidentiality of the participants and complied with the ethical principles established in the Declaration of Helsinki. The confidentiality of the collected data was guaranteed, and strict data protection measures were implemented to ensure that the information was accessible only to the research team. The data were stored on a password-protected computer and will be deleted after five years. The project was approved by the Ethics Committee of the Universidad Católica Sedes Sapientiae (UCSS) and the Ethics Committee of the Hospital Nacional de Lima, ensuring compliance with all relevant ethical and legal regulations.

## RESULTS

In Table 1, it can be observed that among patients with HC, 37 (59.7%) were male and 25 (40.3%) were female, while in the control group, 53 (42.7%) were male and 71 (57.3%) were female. Regarding age, 45 (72.6%) of the cases were under 60 years old and 17 (27.4%) were over 60 years old, compared to 53 (42.7%) and 71 (57.3%) in the controls, respectively. The distribution by area of residence showed that 60 (96.8%) of the cases and 120 (96.8%) of the controls resided in urban areas. Concerning health insurance, 56 (90.3%) of the cases and 111 (89.5%) of the controls had health insurance. The duration of illness less than 10 years was recorded in 47 (75.8%) of the cases and 63 (50.8%) of the controls. The presence of comorbidities was observed in 37 (59.7%) of the cases and 87 (70.2%) of the controls. Regarding medication adherence, 49 (79.0%) of the cases did not adhere to the treatment, compared to 52 (41.9%) of the controls.

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**Table 1.** Sociodemographic characteristics and medical history in diabetic adults with hyperglycemic crises (cases) and without hyperglycemic crises (controls) treated in the emergency unit of a General Hospital in Lima

| Variables | Cases (n=62) | Controls (n=124) | Total (n=186) | p-value |
|---|---|---|---|---|
| **Gender** | | | | 0.029* |
| Male | 37 (59.7 %) | 53 (42.7 %) | 90 (48.4 %) | |
| Female | 25 (40.3 %) | 71 (57.3 %) | 96 (51.6 %) | |
| **Age** | | | | <0.001* |
| < 60 years | 45 (72.6 %) | 53 (42.7 %) | 98 (52.7 %) | |
| ≥ 60 years | 17 (27.4 %) | 71 (57.3 %) | 88 (47.3 %) | |
| **Area of residence** | | | | >0.999† |
| Urban | 60 (96.8 %) | 120 (96.8 %) | 180 (96.8 %) | |
| Rural | 2 (3.2 %) | 4 (3.2 %) | 6 (3.2 %) | |

| | | | | |
|---|---|---|---|---|
| **Health insurance** | | | | 0.864* |
| Absence | 6 (9.7 %) | 13 (10.5 %) | 19 (10.2 %) | |
| Presence | 56 (90.3 %) | 111 (89.5 %) | 167 (89.8 %) | |
| **Duration of illness** | | | | 0.001* |
| < 10 years | 47 (75.8 %) | 63 (50.8 %) | 110 (59.1 %) | |
| ≥ 10 years | 15 (24.2 %) | 61 (49.2 %) | 76 (40.9 %) | |
| **Comorbidity** | | | | 0.153* |
| Presence | 37 (59.7 %) | 87 (70.2 %) | 124 (66.7 %) | |
| Absence | 25 (40.3 %) | 37 (29.8 %) | 62 (33.3 %) | |
| **Acute Infectious Process** | | | | 0.085* |
| Presence | 34 (54.8 %) | 84 (67.7 %) | 118 (63.4 %) | |
| Absence | 28 (45.2 %) | 40 (32.3 %) | 68 (36.6 %) | |
| **Medication Adherence** | | | | <0.001* |
| Non-adherence | 49 (79.0 %) | 52 (41.9 %) | 101 (54.3 %) | |
| Adherence | 13 (21.0 %) | 72 (58.1 %) | 85 (45.7 %) | |

* Chi-square test
† Fisher's exact text

In Table 2, it can be observed that several factors are associated with HC in diabetic adults. Male gender presents an ORc of 1.98 (95% CI 1.07-3.69, p=0.029), while age under 60 years shows an ORc of 3.55 (95% CI 1.83-6.87, p<0.001). Duration of illness less than 10 years is also associated with an ORc of 3.03 (95% CI 1.54-5.99, p=0.001). Additionally, non-adherence to medication presents an ORc of 5.22 (95% CI 2.57-10.59, p<0.001). Other factors such as area of residence, health insurance, comorbidity, and acute infectious process did not show a significant association with HC.

**Table 2.** Bivariate analysis of factors associated with hyperglycemic crises in diabetic adults treated in the emergency unit of a General Hospital in Lima.

| Variables | ORc | CI 95 % | p-value |
|---|---|---|---|
| Gender | 1.98 | 1.07-3.69 | 0.029 |
| Age < 60 years | 3.55 | 1.83-6.87 | <0.001 |
| Area of Residence | 1.00 | 0.18-5.62 | >0.999 |
| Health Insurance | 0.92 | 0.33-2.54 | 0.864 |
| Duration of illness < 10 years | 3.03 | 1.54-5.99 | 0.001 |
| Comorbidity | 0.63 | 0.33-1.19 | 0.153 |
| Acute Infectious Process | 0.58 | 0.31-1.08 | 0.085 |
| Non-adherence to Medication | 5.22 | 2.57-10.59 | <0.001 |

Orc: Crude Odds Ratio. CI 95%: Confidence Interval to 95%

In Table 3, it can be observed that several factors are associated with HC in diabetic adults after performing a multivariate analysis. Age under 60 years presents an ORa of 2.85 (95% CI 1.41-5.79, p=0.004), indicating a significant association. Similarly, non-adherence to medication shows an ORa of 3.87 (95% CI 1.84-8.18, p<0.001). Although duration of illness less than 10 years presented an ORa of 2.01 (95% CI 0.95-4.25), this result was not statistically significant (p=0.067). Male gender did not show a significant association with an ORa of 1.71 (95% CI 0.90-3.26, p=0.462).

**Table 3.** Multivariate analysis of factors associated with hyperglycemic crises in diabetic adults treated in the emergency unit of a General Hospital in Lima.

| Variables | ORa | CI 95 % | p-value |
|---|---|---|---|
| Gender | 1.71 | 0.90-3.26 | 0.462 |
| Age < 60 years | 2.85 | 1.41-5.79 | 0.004 |
| Duration of illness < 10 years | 2.01 | 0.95-4.25 | 0.067 |
| Non-adherence to medication | 3.87 | 1.84-8.18 | <0.001 |

Ora: Adjusted Odds Ratio. CI 95%: Confidence Interval to 95%

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## DISCUSSION

The results obtained in this study show that there is a higher chance of developing an HC in males in the bivariate analysis but not in the multivariate analysis. According to the National Epidemiology Center, DM has a higher prevalence in females [9]; however, men experience more severe complications [10]. This result does not align with the study by Condori Zevallos [8], which found a higher proportion of males in the group of cases with HC among hospitalized diabetic patients in a hospital in Arequipa, Peru. Similarly, a study conducted in the United States in adults with diabetes and end-stage renal disease found that women have a 44% higher risk of developing HC compared to men (IRR: 1.44, 95% CI: 1.35–1.54, p<0.001)[11].

The results of other studies suggest that men may have disorganized behaviors and less rigorous management of their treatment, which precipitates HC. Factors such as non-adherence to insulin and comorbidities are more frequent in men, who, despite a higher prevalence of DM in women, present more severe complications due to physiological and behavioral factors[1,2]. Diabetic patients under 60 years of age have a higher chance of developing an HC, which could be due to the inclusion of type 1 diabetes patients in this study. In type 2 diabetes patients, it has been observed that the risk of acute complications such as HC decreases with age [11]; whereas in type 1 diabetes patients, most complications such as DKA or HHS are observed in young adults between 18 and 44 years[2].

It is important to highlight the relevance of the early appearance of risk factors for developing type 2 diabetes in young people. Type 2 diabetes has shifted from being a disease observed in adults to occurring in younger age groups, primarily associated with an increase in obesity and physical inactivity [12]. Studies have reported on the global burden and trend of diabetes from 1990 to 2017, as well as on diabetes mortality and trends before the age of 25, 1990-2019. Indeed, complications can also be more frequent in this patient group[13].

Regarding the area of residence, no association was found, probably because the study was conducted in a capital city hospital, and most participants came from urban areas, compared to a minority from rural areas. This result can be attributed to the fact that there are currently more high-complexity hospitals in various regions of the country[14]. Additionally, although there is a socioeconomic disadvantage in rural areas, the contrast with urban lifestyles, characterized by higher

prevalence of sedentary behavior and unhealthy diets, could confer a relative benefit in terms of lower incidence of complications. Studies have found that the prevalence of diabetes and prediabetes is significantly higher in urban areas than in rural areas due to more common obesity, physical inactivity, and unhealthy diets in cities. While urban residents have higher levels of education, they also have higher levels of hypertension and obesity[15,16]. Conversely, other studies have shown that although diabetes mortality rates have improved in urban areas, there have been no significant improvements in rural areas. In these regions, chronic diabetes-related complications persist, which could be associated with fewer opportunities for adequate medical care[17-20].

Regarding health insurance, no significant association was found with HC, likely because the vast majority of patients arrived at the emergency room with some form of health coverage, allowing them access to medical care and medications. This study presents results contrary to the research by Wolf et al.[21], who identified that 69% of diabetics in their sample lacked health insurance, especially in the case of type 2 diabetics. These findings demonstrated statistical significance, particularly in the group of patients with type 2 DM. The disparity in results may be attributed to the specific context of the study, conducted in a low-resource county in the United States, serving a population that lacks insurance and has limited access to health services and medical treatment.

A statistical association between HC and the duration of illness was established only in the bivariate analysis but not in the multivariate analysis. This is similar to the findings of Taboada Torres et al.[22] in their study conducted at the Hospital Nacional de Paraguay. The explanation in this case could be that confounding factors such as treatment adherence or age explain these differences. Additionally, individual variability in response to treatment and glycemic control could dilute the direct relationship between the duration of illness and the frequency of HC in a more complex multivariate analysis[23].

On the other hand, a shorter duration of illness could imply that patients have less knowledge and experience in recognizing the symptoms of acute complications, which could affect the frequency and severity of detected HC.

Regarding comorbidities, no association was found, which could be due to the fact that, despite the presence of one or more comorbidities, these may be under patient control with the support of their relatives. These results differ from those found by La Torre-Alejos et al. [24], who found a significant association between vascular diseases and HC, attributing it to the absence of medical controls for chronic diseases in the analyzed population. In particular, in people with type 1 diabetes, it was observed in a study in Germany that comorbidities increased chronic complications[25].

Regarding infectious processes, no significant association was found, despite a higher percentage of diabetic patients with infectious conditions admitted to the emergency room. This confirms that the patients in the studied sample are more prone to infections, possibly due to a weakened immune system. These findings differ from those of Álvarez Torrecilla et al. [5], Sacoto Flores et al.[6], or Condori Zevallos[8], who identified significant associations. The difference could be attributed to the fact that their samples consisted of older populations with a diagnosis of DM for more than ten years. Additionally, they noted the absence of treatment adherence, which could lead to glycemic imbalance and, therefore, increase the risk of infections and metabolic decompensation.

A statistical association was found with medication adherence, determining that non-adherence could influence the triggering of an HC. This result is attributed to a lack of self-care awareness, misinformation, absence of healthy habits, and medical appointments. This result is similar to that obtained by Condori Zevallos [8], Gordo Remartínez et al.[7], and Taboada Torres et al[22]. This may be because the studied samples have similar characteristics, with a higher number of patients with type 2 DM, unhealthy

lifestyles, and unfavorable behaviors for their well-being. Based on these results, it is recommended to strengthen health education programs for type 2 diabetes patients and develop more rigorous follow-up strategies, public awareness campaigns, access to community resources, and improve healthcare professional training to ensure better treatment adherence and prevention of acute complications.

The study's limitations include that the design does not allow for establishing a temporal sequence between exposure and effect, as well as the presence of selection biases and the possible lack of representativeness of the sample, given that the data come from a single hospital. Additionally, the retrospective nature of the study depends on the quality and completeness of the reviewed medical records, which could introduce information biases.

## CONCLUSION

This study found a statistically significant association between age and non-adherence to medication with HC, suggesting that these could be contributing factors for this population developing an acute complication. It is important to highlight that healthcare professionals must work together to prevent these patients from being admitted to the emergency room and strengthen the already established guidelines to achieve an informed, empowered, and healthy population.

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**Authorship Contribution:** MLB participated in the conception and design of the article, data collection, analysis and interpretation of data, drafting of the article, critical review of the article, and approval of the final version. DACS participated in the conception and design of the article, analysis and interpretation of data, drafting of the article, critical review of the article, and approval of the final version.

**Funding:** Self-funded.

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**Conflict of Interest:** The authors declare no conflict of interest.

**Received:** December 13, 2023.
**Approved:** April 29, 2024.

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