

Glycated hemoglobin with $\geq 7.0\%$ results in patients from a Regional Hospital in Costa Rica

Abstract

Objective: Analyze the HbA1c results from patients attached to Ciudad Quesada health area that received attention in the clinical laboratory from San Carlos' Hospital during 2021 and 2022.

Methods: Data from HbA1c values $>7.0\%$ was collected monthly from patients attached to Ciudad Quesada health area, from which also sex, age and EBAIS was registered. The information was further analyzed using Microsoft Excel and the statistics program R studio.

Results: For the year 2021 a total of 2104 results of patients with HbA1c $\geq 7.0\%$ were accounted, as for 2022 the total was of 1656, where the greater frequency was in women. In 2021 most of the patients with $\geq 7.0\%$ HbA1c receive attention in San Pablo's EBAIS, while in 2022 it was in San Juan's EBAIS.

Conclusions: The greater number of people with HbA1c values over or equal to 7% that belong to Ciudad Quesada's healthcare area are women. The results might underestimate the real number of poor controlled patients because the years from which the data was collected correspond with the time the COVID-19 pandemic was ongoing. The age group corresponding with people between 51-70 years old are the ones most frequently found with the values of interest. Further studies must be made in order to determine the factors why these patients have such a poor blood glucose control.

Keywords: glycated hemoglobin, diabetes, healthcare, multifactorial disease, HbA1c

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Abbreviations: CCSS, caja costarricense del seguro social; NGSP, national glycohemoglobin standardization program; HPLC, high performance liquid chromatography; EBAIS, equipo básico de atención integral en salud; ADA, American diabetes association

Introduction

The glycated hemoglobin is formed *in vivo* by the non-enzymatic addition of glucose to the hemoglobin molecules. Specifically, the HbA1c is a stable variant of hemoglobin, which can be separated thanks to its charge and that is also formed mainly by glycohemoglobin.¹ Its determination in the clinical laboratory allows to measure the amount of hemoglobin that has suffered the glycation process in blood, this also works as a great marker to determine if the blood glucose control has been appropriate in the last 3 months. Specifically in Costa Rica, the Caja Costarricense del Seguro Social (CCSS) in its "Guide for the attention of diabetic type 2 patients" establishes a value of HbA1c lower than 7% to indicate that there is a good control, while values between 7% and 8% are considered a regular control, and those above 8% are associated with a bad diabetes control.^{2,3} It is known that there are different complications associated with diabetes, that's why, having an adequate management of blood glucose levels is fundamental in the control of this disease. Between the main acute complications, we can mention the diabetic ketoacidosis, which is characterized for presenting a hyperglycemic state, metabolic acidosis and ketosis; also, according to the seriousness of the case it can lead to a hypovolemic shock scenario. The hyperosmolar hyperglycemic state is another of the complications, in which there's hyperglycemia with extremely high glucose values, ketosis is absent, and it also occurs an osmolarity rise in plasma. In this case there is severe dehydration which cannot be compensated with fluids or liquids ingestion, in addition the patient can present alterations in the consciousness levels until getting into a coma state. We can also mention hypoglycemia, in which blood

glucose values come down to levels under 60 mg/dL generating scenarios that can be mild, moderate or severe; in the last one you can also see severe neurological disorders such as coma or seizures.⁴

As part of the goals a diabetic patient must reach in a therapeutic process, there is keeping a HbA1c value under 7%. However, there are different reasons that cause difficulties to accomplish this goal. Between the different factors that affect the metabolic control of the patients we can quote:

- I. Personal: age, beta pancreatic cell mal function, insulin resistance increase.
- II. Treatment: expiry date of the drugs, mistakes with insulin storage, insulin administration and dosage mistakes.
- III. Habits: non healthy eating, lack of physical activity, lack of treatment adherence, inadequate self-control.
- IV. Others: use of hyperglycemic drugs, infectious processes, concomitant diseases, psychiatric disorders, family and social problems, etc.⁴

The final idea of having an optimal diabetes control is that the patient can diminish the associated symptoms known, improve life quality, prevent acute and long-term complications, doing an adequate treatment of complications and diminishing the disease's mortality.²

To determine the HbA1c it is used the HPLC, or High-Performance Liquid Chromatography technique. It allows to separate the different hemoglobin fractions, in which we can find the A1c fraction which is the most important in control and follow up of diabetic patients. This methodology is widely used all over the world.^{5,6} The NGSP or National Glycohemoglobin Standardization Program has as main purpose to standardize the HbA1c test results, so that they are comparable with other existent assays such as the DCCT and UKPDS; being them the

ones who established the relationship between the HbA1c levels and the risk of complications due to hyperglycemia. The HPLC technique for HbA1c determination is one of the NGSP known, traceable and standardized methods that allows to follow up and diagnose.^{7,8} The idea of this work is to determine the number of patients with HbA1c values equal or over 7.0%, which is considered in Costa Rica as a poor control of the disease. Also, through the analysis of the data it is important to find out if there's a particular age group affected by these inadequate numbers; and if there's a difference between men and women. Further information might be valuable to determine if there any kind of external factors associated to the lack of control of the HbA1c values.

Materials and methods

Ciudad Quesada is a district that belongs to San Carlos, a city from Costa Rica's province called Alajuela. Its geographical surface is 144 km². The population attached to Ciudad Quesada's healthcare area for the year 2021 was 51 460 patients according to data from CCSS.⁹ In order to do this retrospective and transversal study, the results of HbA1c with values $\geq 7.0\%$ from patients belonging to the different EBAIS that conform Ciudad Quesada's Health Area, and that received attention at the clinical laboratory from San Carlos Hospital, were compiled during 2021 and 2022. The studied variables were age and sex in relation to the HbA1c values. The data collection was made monthly, from January to December of both years. In order to do this, the HbA1c percentage was registered, as well as age, sex and EBAIS from each of the patients attached to during the time of analysis. This was made in a Microsoft Excel document that was divided with the different EBAIS and with the different months of each year. All the information was obtained through the laboratory informatic system called LabCore, and it was charted in the Microsoft Excel document to be analyzed. Additionally, the program R Studio was used for the graphic representation of the data. The graphic was made to compare age and sex to the HbA1c values. Since the data was collected monthly, there was information about the frequency in each month. Inside the laboratory, the total blood samples collected with EDTA were processed using the automatic analyzer called Tosoh G8 which uses the HPLC technique, and that allows to obtain the HbA1c results as percentage. The laboratory is a participant of the external quality control program called RIQAS, this allows to have a great confidence in the results we get. Also, there is an internal quality control that's made daily, and it also guarantees the quality of the determinations. In this specific case, the samples whose values were under 7% were excluded from the study, indifferently the patients age or sex. It was not necessary to use an informed consent since all the data was collected from the laboratory's informatic system and not directly from the patients.

Results

A total of 2104 results from patients with HbA1c $\geq 7.0\%$ were accounted during 2021; while in 2022 the total was of 1656. From the analyzed data it is seen that for 2021 the month in which most patients with values $\geq 7.0\%$ was March, with a total of 261; followed by April with 200 patients. In 2021 the difference according to sex was remarkable, being women the ones who got these values more frequently. The total was of 1262 women versus 842 men Figure 1. As for the EBAIS distribution, San Pablo's EBAIS is the one with the greater number of patients that registered the values of interest, with a total of 222. Next on the list is San Juan with 219 and Dulce Nombre with 192, being these three the EBAIS with the most frequent altered values. In 2022 the month with more patients whose values were

equal or higher than 7% was December with 235 patients; however, there was also a peak in May with 222.

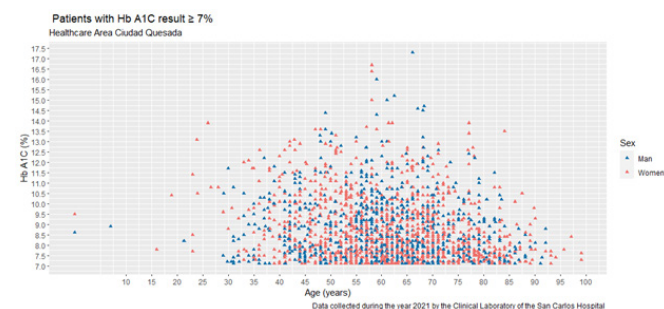


Figure 1 Distribution of patients with HbA1c values $\geq 7.0\%$ according to sex and age in the year 2021.

According to sex, the distribution remained the same as in 2021, being the number of female patients higher, with a total of 999. For male patients the number observed was even lower than the registered one for 2021, with a total of 657 Figure 2. The EBAIS of San Juan remained part of the ones with higher number of patients with HbA1c values $\geq 7.0\%$ with a total of 239, taking the first place in year 2022. In second place is EBAIS San Martin with 166 and Ciudad Quesada with 160. Finally, according to the different groups of ages the patients corresponding to 61- 70 years old are the ones in which this kind of values were found the greatest number of times. The next group was the ones between 51-60 years old for the year 2021. In 2022 the behavior remained the same, with the group of 61-70 years with a total of 539 and followed by the group of 51-60 years with 406 patients in total. The corresponding percentages found were 30% for 61-70 years old and 27% for 51-60 years in 2021, while in 2022 it was 33% and 25% for the same groups of age (Table 1 & 2).

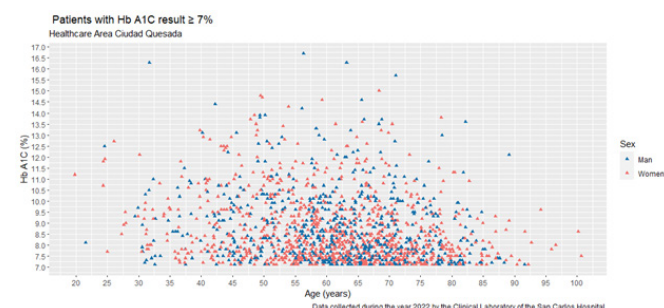


Figure 2 Distribution of patients with HbA1c values $\geq 7.0\%$ according to sex and age in the year 2022.

Table 1 Frequency of HbA1c values $\geq 7.0\%$ according to the different groups of ages in 2021

Age group	Total	Percentage
0-10	3	0
20-Nov	2	0
21 - 30	16	1
31 - 40	99	5
41- 50	297	14
51- 60	573	27
61 - 70	626	30
71 - 80	350	17
81 - 90	125	6
91 - 100	13	1
101 - over	0	0
Total	2104	100

Table 2 Frequency of HbA1c values $\geq 7.0\%$ according to the different groups of ages in 2022

Age group	Total	Percentage
0-10	0	0
20-Nov	1	0
21 - 30	15	1
31 - 40	83	5
41- 50	225	14
51- 60	406	25
61 - 70	539	33
71 - 80	297	18
81 - 90	80	5
91 - 100	9	1
101 -	1	0
Total	1656	100

Discussion

Diabetes Mellitus is a healthcare problem that constitutes a mayor challenge when it comes to handling the disease. In Costa Rica, the CCSS, as the main institution in charge of public healthcare, has a guide to follow up and handle patients with type 2 diabetes. This guide establishes as a goal, that diabetic patients should have HbA1c values under 7% in order to have an adequate control. The American Diabetes Association (ADA) proposes that a value under 7% of HbA1c might be used as a therapeutic goal in diabetic patients, since it has been demonstrated that it decreases the risks of having a neuropathy for example, or micro and macrovascular complications.¹⁰ This value is established due to the correlation there is between the HbA1c values as a percentage and the estimated glucose blood value. According to this a HbA1c value of 7% equals to an estimated of 154 mg/dL of blood glucose (NGSP). As the glycated hemoglobin value gets higher, the estimated blood glucose gets higher as well until it reaches values around 300 mg/dL (NGSP). If a patient usually has glycated hemoglobin values above 7%, this means that the blood glucose levels have also been high, which is known that can lead to acute and chronic complications. Being this a multifactorial disease, it is very important to take into consideration the social determinants of the pathology, because some factors such as school level, economic income, family support and sedentary lifestyle for example, can make a huge difference when it comes to control. In the case of the studied population, there is evidence that women were more affected, since in both 2021 and 2022 there was a bigger proportion of female patients with values over 7%. This could be related to a series of factors that are well known to influence diabetes control.

In a study about the behavior of diabetes in Costa Rica, it was determined that in the country the incidence rate is 3 times higher in women than it is in men¹¹, and according to the results of the investigation there's evidence that in Costa Rica most of the diabetic patients are female, being them the ones with a worst glycemic control which is evidenced by the HbA1c values over 7%. According to Kautzky-Willer, Harreiter & Pacini, in diabetes mellitus there are different factors that generate a greater predisposition in women to have this disease, between these factors there are the genetic and epigenetic mechanisms, sedentary lifestyle, nutritional factors, body fat distribution, feminine sexual hormones, stress, among others¹². This is also reflected in the present study, were most of the affected patients were women. It is important to take in consideration that the data collected for this study corresponds with two years in which Costa Rica and the entire world faced the COVID-19 pandemic, which

is why the data can present an important bias since a lot of patients stopped assisting to health care centers as a preventive measure to avoid the virus infection. Also, due to government recommendations, a lot of people stayed home, which could also influence in a negative way the glycemic control due to stress, anxiety and the constant access to food.

According to the months with higher frequency, there is no seasonal nature related since both years presented different months with a higher quantity of altered values. However, a bigger sample should be analyzed in order to rule out or confirm a seasonal nature. It's important to emphasize that in 2022 there were two peaks, corresponding with two different months in which a big number of patients with values over 7% were detected.

During the last semester of 2022, the country starts lifting all the restrictions due to the pandemic, and a call to take care of people with chronic diseases that during 2021 and 2022 had a poor follow up was made, which is why in the last trimester of 2022 there is a rise in the detection of people with an inadequate control of their blood glucose values. On the other hand, it is well known that women have an active participation y and more likely to visit the doctor, which is why the results confirm the statistical data. With the extracted results from this study, it cannot be confirmed that women are the ones with a worst blood glucose management regarding men; in order to do this type of analysis it is necessary to use a sample of diabetic people, with the same number or men and women and then do a follow up of them. But it's important to highlight that the behavior matches what previous studies of how the incidence of diabetes behaves in Costa Rica.

Regarding the detection of diabetic patients with a poor control of the blood glucose levels in the different EBAIS that make up Ciudad Quesada's health care area, EBAIS San Juan was both in 2021 and 2022 one of the centers with the most patients that had HbA1c values $\geq 7.0\%$. This result might be due to factors such as: higher number of patients that attend to this EBAIS in comparison of the other 12, higher installed capacity to take care of the patients, or a combination of both factors. This piece of information could be used for further investigation in which it is determined what are the factors, such as socioeconomic level of the population, that match best with the patients presenting the worst control values of HbA1c. Also, it is very important to do further research to find out what factors are related to the fact that the population between 51-70 years are the ones mostly affected by these altered values. Combined they sum up to 57% in 2021 and 58% in 2022, of the patients with HbA1c values over 7%. This age group is known to have certain behaviors that can be related to these results, such as bad eating habits, lack of physical activity, lack of an adequate insulin use, amongst other factors. But, in order to determine these further studies must be made, so that the healthcare area can establish control programs to directly attack the determinant factors. It is also important that no similar studies were found in the literature. There are previous studies that relate the HbA1c values with the incidence of hemoglobin variants for example, but there was no evidence of studies that correlate the HbA1c values with age or sex of the patients in Costa Rica.

Conclusion

From the present observational study and the data analysis, it can be concluded that the greater number of people with HbA1c values over or equal to 7% that belong to Ciudad Quesada's healthcare area are women, but this doesn't mean that women are the ones with the worst blood glucose control, other than them being the ones that are more likely to go to their medical follow ups. The data obtained can

underestimate the real number of patients with a poor management of the blood glucose values due to the confinement caused by COVID-19 pandemic, which is why we can speculate the real number might as well be higher. Once the government softened the restrictive measures they once had to stop the Sars-CoV-2 virus spread, and started to improve the attention of patients with chronic diseases during the last semester of 2022 it allowed for more people whose values were $\geq 7.0\%$ to be captured during the last trimester of the ongoing year. To know the reason why some of the EBAIS have a greater ability to detect these cases of patients with a poor control of diabetes, it is necessary to amplify the study in order to tackle: total of population attached to each EBAIS and the percentage of that population that has diabetes, know the socioeconomic conditions of the inhabitants and determine the installed capacity each EBAIS has for patients' attention. Also, knowing there are specific age groups that are more likely to have these out-of-control values, it's important to establish strategies such as stricter control, education, good eating habits, and others. This in order to accomplish the goal of a value under 7% which is known to reflect in a better life quality.

Acknowledgments

None.

Conflicts of interest

The authors declare there is no conflict of interest in this job.

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