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Research Article

Hyperglycemia as a Sequel to Covid-19

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Abstract

Background: SARS-CoV-2 has generated a severe economic, social and health crisis throughout the world. Multiple experimental and clinical studies have suggested that in addition to generating a pulmonary clinical presentation, it can also cause lesions in different systems. The present study seeks to associate that SARS-CoV-2 infection can generate a hyperglycemicstate in patients without a previous diagnosis of Diabetes Mellitus, as well as to find the prevalence of this complication in specific groups of the population.

Overall Objective: To determine the prevalence of hyperglycemia in the subjects who studied COVID-19 of the Family Medicine unit No 32.

Material and methods: An observational, descriptive, cross-sectional and retrospective study was developed with a non-probabilistic sampling of consecutive cases in the population of patients with COVID-19 of the Family Medicine Unit No. 32 of the Mexican Institute of Social Security with an age range of 18 - 65 years. Obtaining a sample of 152 participants who met the inclusion criteria.

Results: A prevalence of 30.26% was found in the participants who presented post-COVID hyperglycemic figures.

Conclusion: In the present study we can conclude that there was an alteration in post-COVID serum glucose levels without the use of steroids, which is why future follow-up is suggested for patients who suffered from COVID-19 to monitor the possible onset of pre-diabetes or diabetes.

Keywords: Beta coronavirus; Coronavirus infections; Hyperglycemia

Introduction

The current COVID-19 pandemic is caused by a mutant strain of corona virus. Starting in China at the end of December 2019, in the province of Hubei, Wuhan; where a group of 27 cases of pneumonia of unknown etiology, with seven seriously ill patients, was reported [1]. The severity of illness has ranged from a mild self-limiting flu-like illness to fulminant pneumonia, respiratory failure, and death. The population that is generally vulnerable to this corona virus is older adults and patients with certain diseases, including high blood pressure and Diabetes Mellitus, are more vulnerable to SARS-CoV-2 [2].

During the course of the pandemic, multiple experimental and clinical studies have been carried out that have suggested that SARS-CoV-2, apart from generating a pulmonary clinical presentation, can also cause lesions in multiple systems [3].

Hyperglycemia is frequently reported in COVID-19 [4], occurring in 50% of patients hospitalized for COVID-19, when the prevalence of pre-existing Diabetes Mellitus in the same population is approximately 7-10% [5]. A recent study explored the physiological model for SARS-CoV- 2 resulting in hyperglycemia and acute diabetes [6], which may change the course of the disease in patients with COVID-19 as a risk factor for severe disease [7].

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There are two hypotheses for which hyperglycemia is particularly acute. The first is that acute hyperglycemia is accompanied by a large increase in inflammatory mediators caused by interleukin-6 [8], triggering an inflammatory and stress response with increased cortisol, sympathetic activity, and growth hormone. This will induce a state of insulin resistance leading to hyperglycemia [9].

The second is related to its union with an Angiotensin Converting Enzyme (ACE2) in the type 2 pneumocyte, through its glycoprotein S [8]. The S glycoprotein of the virus activates ACE 2 as a receptor for entry into the pancreas [10].

The SARS-CoV-2 corona virus penetrates the pancreatic islets and damages the beta cells, which would produce a deficiency in insulin secretion. This would lead to an aggravation in people with previous Diabetes and induce acute hyperglycemia even in people without Diabetes Mellitus [11].

The Spanish Society of Internal Medicine conducted a study of 11,312 patients, classifying them into three groups, according to blood glucose levels, at admission: <140 mg/dl, 140-180 mg/dl and >180 mg/dl. Hospital mortality rates were 15.7% for patients with blood glucose <140 mg/dl, 33.7% for those with 140-180 mg/dl, and 41.1% for patients with >180 mg/dl. Blood glucose [12].

In a review of studies published in the United States, SARS-CoV-2 was shown to cause higher fasting plasma glucose levels and pancreatic beta-cell damage was incriminated as a cause of the development of "Acute Diabetes" [10].

Multiple studies have sought a relationship between hyperglycemia levels and the severity of the infection, finding that patients with COVID-19 without Diabetes Mellitus had a relatively higher increase in blood glucose, regardless of the severity of the infection, compared to with COVID-19 patients with Diabetes Mellitus [13].

In studies of glycemic characteristics of 1,122 hospitalized patients with COVID-19, he reported that 257 patients had uncontrolled hyperglycemia, acute diabetes could represent a complication of a viral infection in pancreatic islet cells [14].

In a cohort of 184 patients, 88 patients with Diabetes Mellitus (47.8%) and 96 with uncontrolled hyperglycemia (52.2%). Patients with uncontrolled hyperglycemia had a longer duration from admission to death (8.4 vs 6.0 days, $p < 0.001$), of the 184 patients who died or were discharged, 40 of 96 patients with Uncontrolled hyperglycemia (41.7%) died compared to 13 of 88 patients with Diabetes Mellitus (14.8%, $p < 0.001$) [15].

In China, it was carried out in a population of 166 patients divided into three groups depending on their glycemic figures and previous history of diabetes. This study suggests that COVID-19 patients with secondary hyperglycemia constitute another population with a poor prognosis. Adding a significantly higher hospital mortality rate for patients with new hyperglycemia, who also had worse outcomes than patients with a previous history of diabetes and subjects with normoglycemia [16].

Material and Methods

An observational, descriptive, retrospective cross-sectional study was developed in a population of patients with COVID-19 from the Family Medicine Unit No.32 of the Mexican Institute of Social Security with an age range of 18-65 years.

The population was made up of patients who were assigned to the Family Medicine Unit No.32, and who met the inclusion criteria.

Inclusion criteria

Be attached to the Family Medicine Unit No. 32 Age 18-65 years.

Participants without previous diagnosis of Type 1 or 2 Diabetes Mellitus prior to COVID-19 infection.

Positive SARS-CoV-2 test result Have pre- and post-infection glucose laboratory results.

Exclusion criteria

Not being pregnant during the infection Participant Death Steroid use. Hospitalized Participants

Elimination criteria

Incomplete files.

The study considered all patients who met the aforementioned selection criteria, in the established place and time, through a non-probabilistic sampling of consecutive cases, obtaining a sample of 152 participants who met the inclusion criteria.

A review of the electronic files of the Family Medicine Unit No.32 was carried out.

In them, information was obtained regarding the beneficiaries assigned to the unit, the social security number, the pathological history, if it was managed on an outpatient basis and the result of the confirmatory test of these, from participants who met the selection criteria. in a period of time from July 2020 to March June 2021.

Subsequently, the SILAB system of the unit was used, where the laboratory results of the selected participants were searched and a comparison of the glycemic figures before and after the COVID-19 infection was made.

Results

An observational, descriptive, cross-sectional and retrospective study was carried out with a non-probabilistic sampling of consecutive cases, obtaining a sample of 152 participants who met the inclusion criteria during the years 2020-2021, with a composition of 25% (N =38) men and 75% (N=114) women (Table 1).

Age was distributed from 18 to 65 years with a mean of 41.86 years and a SD of 11.85. Glycemic Variation in Normoglycemic Participants they present a mean of 0.52 mg/dl, and a SD of 9.93 and an average of glycemic variation with a mean of 0.01% and a SD of 0.11. Number of characteristic symptoms of COVID-19 that the participant presented at the time of diagnosis presented a mean of 6.69 symptoms and SD 2.92 (Table 2).

In the study, it was observed that 30.26% (N=46) resulted in hyperglycemia after SARS-CoV-2 infection and 69.74% (N=106) with a 95% CI (61.77-76.92) remained normoglycemic (Table 3).

An association was made between the qualitative variables of gender and the final glycemic status of the participants, where we assessed the susceptibility between belonging to one gender and presenting or not hyperglycemia. We can observe that hyperglycemia occurred more in men with 42.11% (N=16)

compared to women 26.32% (N=30); we can corroborate it with the OR of 2.03 (CI: 0.9456 - 4.3855) and a p 0.03, presenting a X^2 corrected to 0.10 and the exact Fisher test of 0.10 (Table 4).

An association of the variables works status and final glycemic status was made; employment status was divided into three categories: employed 73.68% (N=112), unemployed 25% (N=38), and retired 1.32% (N=2).

We observed that the participants who currently have a job are the ones that make up the largest number of total cases of hyperglycemia in the sample with 69.57% (N=32). However, when compared with the other two categories, the employees are the ones with the least tendency to hyperglycemia; In the category of retirees, although it presents a small population of 2 members, all its participants presented hyperglycemia. In unemployed people it has a probability of generating hyperglycemia with 31.58% (N=12). We obtained a X^2 of 4.79, a p of 0.09 and a Fisher exact test of 0.13 (Table 5).

When analyzing the variables of labor status associated with the gender variable of the participants, it was observed that in the case of men, the group of employees were the ones that presented a lower probability of suffering from hyperglycemia due to labor status with 35.71%, the group of retirees I present a greater probability of suffering from hyperglycemia when presenting in 100% (N=2) of the cases of the sample, with the group of unemployed they presented a probability of 50% in presenting both hyperglycemic figures .

In the case of women, it was found that both groups have a similar probability of suffering from hyperglycemia, with the group of unemployed women being more likely with 26.67% (N=8) than the group of employees with 26.19% (N=22) the cases.

In the study, the participants were grouped by age groups regardless of sex or employment status (N=152), in 8 age ranges. We observed that group 5 was more susceptible to contracting SARS-CoV-2 since this age group represents 22.37% (N=34) of cases in the sample and this same age group was the one that showed a higher prevalence for present hyperglycemia with 26.06% (N=12) of the sample. Group 1 did not present any case of hyperglycemia and group 4 was the one with the highest probability of hyperglycemia by age group with 50% (N=10) of the cases (Table 6).

With the same age groups, a table of association of age group with glycemic variation was made in normoglycemic participants (N=106), where 49.06% (N=52) presented an increase in glycemia in relation to their result. Prior to infection and the other 50.94% (N=54) decreased. We observed that group 8 was the one that presented a greater upward glycemic variation in Post-COVID glycaemia since 100% (N=8) of it presented glycemic elevations. Group 1 was the age group that presented the greatest downward glycemic variation with 80% (N=8) of the members. There is a p of 0.06 and an exact Fisher's test of 0.045 with statistical significance (Table 7).

The number of symptoms suffered was associated with the final glycemic status of the participants, observing that the participants who presented 7 symptoms had a higher probability of hyperglycemia with 21.74% (N=10), followed by the participants who presented 5 and 8 symptoms with 13.04%. Obtaining a p of 0.02 with statistical significance (Table 8).

Finally, a grouping of the variable time elapsed in weeks between the time of diagnosis was made, having a total of 4 groups and the Post-COVID blood glucose figure, dividing it into two groups according to blood glucose, the first of a blood glucose <99.9mg/ dl and a blood glucose >100mg/dl, to assess whether the time elapsed since the diagnosis and the Post-COVID figure play a role in the level of blood glucose that we can obtain.

We can observe that after week 33 there is a decrease in cases of hyperglycemia up to 91.30% (N=42) (Table 9).

Table 1: Frequency table of the qualitative variable of sex.

Sex	F	%	CI 95%	
female	114	75.00%	67.34%	81.66%
Male	38	25.00%	18.34%	32.66%

epi source info V. 7.2 F: frequency IC: Confidence interval.

Table 2: Table of measures of central tendency of quantitative variables.

	Obs	Half	Median	Fashion	Var	OF	Total
Age	152	41.8684	43.5	Four. Five	140.6448	11.8594	6364
No SYMPTOMS	152	6.6974	6	6	8.5303	2.9207	1018
Pre -Covid figure	152	90.9421	92.5	98.2	60.0629	7.75	13823.2
Post-Covid Figure	152	96.3118	93.35	83	193.7316	13.9188	14639.4
Variation Figure	152	5.3697	5.55	9	186.0464	13.6399	816.2
Variation Average	152	0.063	0.0603	- 0.2381	0.0223	0.1495	9.5734
Time In Weeks Between Dx And Post -Covid Result	152	19.1684	17.65	23.1	131.35	11.4608	2913.6
Pre -Covid figure (Normoglycemic)	106	89.1434	90	76	65.7731	8.1101	9449.2
Post-Covid Figure (Normoglycemic)	106	89.7057	91	83	47.5819	6,898	9508.8
Variation Figure (Normoglycemic)	106	0.5623	-0.1	9	98.7997	9.9398	59.6
Variation Average (Normoglycemic)	106	0.0141	-0.0011	-0.2381	0.0139	0.1178	1.4946
epi source info V. 7.2 Var: Variable, SD: Standard Deviation							

Table 3: Frequency table of the qualitative variable of final glycemic status.

hyperglycemia	46	30.26%	23.08%	38.23%
Normoglycemia	106	69.74%	61.77%	76.92%
epi source info V. 7.2 F: frequency IC: Confidence interval				

ESTADO GLUCEMICO FINAL

SEXO	HIPERGLUCEMIA	NORMOGLUCEMIA	
MASCULINO	16 42.11 % 34.78 %	22 57.89 % 20.75 %	38 100.00 % 25.00 %
FEMENINA	30 26.32 % 65.22 %	84 73.68 % 79.25 %	114 100.00 % 75.00 %
	46 30.26 % 100.00 %	106 69.74 % 100.00 %	152 100.00 % 100.00 %

Single Table Analysis

Odds- and Risk-based parameters

	Estimate	Lower	Upper
Odds ratio	2.0364	0.9456	4.3855
MLE Odds ratio (Mid-P)	2.0261	0.9288	4.3918
Fisher-Exact		0.8715	4.6714
Risk ratio	1.6000	0.9870	2.5937
Risk difference	15.7895	-1.8678	33.4467

Statistical Tests

	X^2	2 Tailed P
Uncorrected	3.3667	0.0665271308
Mantel-Haenszel	3.3445	0.0674281301
Corrected	2.6601	0.1028940125

	1 Tailed P	2 Tailed P
Mid-P Exact	0.0377809577	
Fisher-Exact	0.0532566062	0.1016688755

Table 4: Association between qualitative variables of sex vs final glycemic status.

ESTADO GLUCEMICO FINAL

OCUPACION	HIPERGLUCEMIA	NORMOGLUCEMIA	TOTAL
DESEMPLEADO	12 31.58 % 26.09 %	26 68.42 % 24.53 %	38 100.00 % 25.00 %
EMPLEADO	32 28.57 % 69.57 %	80 71.43 % 75.47 %	112 100.00 % 73.68 %
JUBILADO	2 100.00 % 4.35 %	0 0.00 % 0.00 %	2 100.00 % 1.32 %
TOTAL	46 30.26 % 100.00 %	106 69.74 % 100.00 %	152 100.00 % 100.00 %

Chi-square	df	Probability
4.7917	2	0.0911
Fisher's Exact		0.1374

Table 5: Association between qualitative variables of occupation vs final glycemic status.
epi source info V.7.2

ESTADO GLUCEMICO FINAL

EDAD	HIPERGLUCEMIA	NORMOGLUCEMIA	TOTAL
GRUPO 1 (19-24.9 AÑOS)	0 0.00 % 0.00 %	10 100.00 % 9.43 %	10 100.00 % 6.58 %
GRUPO 2 (25-30.9 AÑOS)	4 16.67 % 8.70 %	20 83.33 % 18.87 %	24 100.00 % 15.79 %
GRUPO 3 (31-36.9 AÑOS)	4 22.22 % 8.70 %	14 77.78 % 13.21 %	18 100.00 % 11.84 %
GRUPO 4 (37-42.9 AÑOS	10 50.00 % 21.74 %	10 50.00 % 9.43 %	20 100.00 % 13.16 %
GRUPO 5 (43-48.9 AÑOS)	12 35.29 % 26.09 %	22 64.71 % 20.75 %	34 100.00 % 22.37 %
GRUPO 6 (49 -54.9 AÑOS)	8 36.36 % 17.39 %	14 63.64 % 13.21 %	22 100.00 % 14.47 %
GRUPO 7 (55-60.9 AÑOS)	6 42.86 % 13.04 %	8 57.14 % 7.55 %	14 100.00 % 9.21 %
GRUPO 8 (61-67 AÑOS)	2 20.00 % 4.35 %	8 80.00 % 7.55 %	10 100.00 % 6.58 %
TOTAL	46 30.26 %	106 69.74 %	152 100.00 %

Chi-square	df	Probability
13.0319	7	0.0713
Fisher's Exact		computing...

Table 6: Association between the qualitative variables of age groups vs final glycemic status.
epi source info V.7.2

VARIACION GLUCEMICA

EDAD	AUMENTO	DISMINUYE	TOTAL
GRUPO 1 (19-24.9 AÑOS)	2 20.00 % 3.85 %	8 80.00 % 14.81 %	10 100.00 % 9.43 %
GRUPO 2 (25-30.9 AÑOS)	12 60.00 % 23.08 %	8 40.00 % 14.81 %	20 100.00 % 18.87 %
GRUPO 3 (31-36.9 AÑOS)	6 42.86 % 11.54 %	8 57.14 % 14.81 %	14 100.00 % 13.21 %
GRUPO 4 (37-42.9 AÑOS)	4 40.00 % 7.69 %	6 60.00 % 11.11 %	10 100.00 % 9.43 %
GRUPO 5 (43-48.9 AÑOS)	10 45.45 % 19.23 %	12 54.55 % 22.22 %	22 100.00 % 20.75 %
GRUPO 6 (49-54.9 AÑOS)	6 42.86 % 11.54 %	8 57.14 % 14.81 %	14 100.00 % 13.21 %
GRUPO 7 (55-60.9 AÑOS)	4 50.00 % 7.69 %	4 50.00 % 7.41 %	8 100.00 % 7.55 %
GRUPO 8 (61-67 AÑOS)	8 100.00 % 15.38 %	0 0.00 % 0.00 %	8 100.00 % 7.55 %
	52	54	106

Chi-square	df	Probability
13.5203	7	0.0604
Fisher's Exact		0.0451

Table 7: Association between the qualitative variables of age groups vs glycemic variation in normoglycemic participants.
epi source info V.7.2

ESTADO GLUCEMICO FINAL

NUMERO DE SINTOMAS	HIPERGLUCEMIA	NORMOGLUCEMIA	TOTAL
1	4 66.67 % 8.70 %	2 33.33 % 1.89 %	6 100.00 % 3.95 %
2	0 0.00 % 0.00 %	4 100.00 % 3.77 %	4 100.00 % 2.63 %
3	0 0.00 % 0.00 %	6 100.00 % 5.66 %	6 100.00 % 3.95 %
4	2 14.29 % 4.35 %	12 85.71 % 11.32 %	14 100.00 % 9.21 %
5	6 33.33 % 13.04 %	12 66.67 % 11.32 %	18 100.00 % 11.84 %
6	4 11.76 % 8.70 %	30 88.24 % 28.30 %	34 100.00 % 22.37 %
7	10 50.00 % 21.74 %	10 50.00 % 9.43 %	20 100.00 % 13.16 %
8	6 33.33 % 13.04 %	12 66.67 % 11.32 %	18 100.00 % 11.84 %
9	2 25.00 % 4.35 %	6 75.00 % 5.66 %	8 100.00 % 5.26 %
10	4 33.33 % 8.70 %	8 66.67 % 7.55 %	12 100.00 % 7.89 %
12	2 50.00 % 4.35 %	2 50.00 % 1.89 %	4 100.00 % 2.63 %
13	2 50.00 % 4.35 %	2 50.00 % 1.89 %	4 100.00 % 2.63 %
15	4 100.00 % 8.70 %	0 0.00 % 0.00 %	4 100.00 % 2.63 %
TOTAL	46 30.26 % 100.00 %	106 69.74 % 100.00 %	152 100.00 % 100.00 %

Chi-square	df	Probability
30.0184	12	0.0028
Fisher's Exact		Cannot compute. Too many iterations.

Table 8: Association between the variables of number of symptoms vs final glycemic status.
epi source info V.7.2

TIEMPO EN SEMANAS	CIFRA POSCOVID_ GRUPO 1 (1- 99.9mg/dl)	GRUPO 2 (100-200mg/dl)	TOTAL
GRUPO 1 (1-16.9 SEMANAS)	52 70.27 % 49.06 %	22 29.73 % 47.83 %	74 100.00 % 48.68 %
GRUPO 2 (17-32.9 SEMANAS)	40 66.67 % 37.74 %	20 33.33 % 43.48 %	60 100.00 % 39.47 %
GRUPO 3 (33-48.9 SEMANAS)	10 83.33 % 9.43 %	2 16.67 % 4.35 %	12 100.00 % 7.89 %
GRUPO 4 (49-64 SEMANAS)	4 66.67 % 3.77 %	2 33.33 % 4.35 %	6 100.00 % 3.95 %
TOTAL	106 69.74 % 100.00 %	46 30.26 % 100.00 %	152 100.00 % 100.00 %

	Chi-square	df	Probability
	1.3559	3	0.7159
Fisher's Exact			0.7450

Table 9: Association between qualitative variables groups of time elapsed since diagnosis and post -covid figure.
epi source info V.7.2

Discussion

Currently, at the time this work was carried out, no studies were found where outpatients were analyzed, focusing on hospitalized patients. A high percentage of participants were found to have hyperglycemia as a complication, being 30.26% of the total study, disagreeing with Sánchez (2020), who informs us in his study that hyperglycemia occurs in 50% of patients hospitalized for COVID-19 and that 10% of them had Diabetes Mellitus prior to infection. It is important to mention that in our population, no participant was hospitalized, this being a risk factor for the appearance of hyperglycemia, nor did they have a previous diagnosis of Diabetes Mellitus.

In our results, we observed that the participants showed an increase in Post-COVID plasma glucose levels, comparing them with their plasma glucose results obtained prior to the infection, where it occurred in 64.47% of the cases. This coincides with what was investigated by Ilias (2021) where they found that patients with COVID-19 without Diabetes Mellitus had a relatively greater increase in blood glucose, regardless of the severity of the infection. Unlike the Ilias study, in which the blood sample was taken at the time of admission to the hospital and monitored during its evolution, our study used the results of laboratories that were in the database before and after infection.

At the time that an association was made regarding the time elapsed from diagnosis and Post-COVID glucose measurement, we can observe that after week 33 there is a decrease in cases of hyperglycemia up to 91.30%, which suggests that with Over time, glycemic levels normalize, in agreement with the work of Thaweerat (2020), where he raises the idea of transient hyperglycemia, however, since the participants were not followed up, it could not be corroborated. Despite the fact that in our study the data were not significant, it would be pertinent to carry out a closer follow-up in the participants who presented hyperglycemia in order to corroborate its existence.

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