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Novel Genomic Variants Sars-Cov-2 and blood glucose in the post-pandemic period: Retrospective epidemiology study

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Abstract

Coronavirus disease 2019 (COVID-19) is a highly infectious illness caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which started in China in December 2019 and rapidly spread across the world became the pandemic disease of the 21st century. Diabetes is a known risk factor for mortality in Coronavirus disease 2019 (COVID-19) patients. SARS-CoV-2 infects peripheral blood monocytes and enhances the expression of angiotensin-converting enzyme 2 (ACE2). We conducted this study to evaluate the impact of glucose morbidities on several events in COVID 19. Thus, the main of this study is to detect the presence of glucose levels in the post-pandemic period, as diabetic people have a higher risk of developing severe illness from COVID-19. This is a retrospective epidemiology study involving patients categorized into three groups to admission Blood Glucose (BG) levels: < 70 mg/dL; 77 – 90 mg/dL; < 99 mg/dL according to standard glycaemic targets in the post pandemic period among 2023 and 2023 y. It was carried out the tracking of 19 genomic variants by accessible via GISAID EpiCoV. About 110 countries shared 25,321 GRA (BA.2.86+BA.2.86.*) genome sequences from sample collection to making these data publicly. Therefore, further studies are needed to better be understanding of measurement in diabetic patients at high risk for COVID-19. New insulin therapy or increased dosing from baseline had not been considered. Genomic tools as Next Generation Sequencing (NGS) for the characterization of viral samples and in genetic engineering for the development of vaccines had been advanced molecular studies during SARS-CoV-2 pandemic.

Keywords: Blood glucose; COVID-19; Diabetes; Genomic variants; SARS-CoV-2

1. Introduction

Coronavirus disease 2019 (COVID-19) is a highly infectious illness caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) which started in China in December 2019 and rapidly spread across the world became the pandemic disease of the 21st century [1, 2]. Currently there is limited knowledge on medical comorbidities corelated glucose and COVID-19 so the main purpose of this study is to detect the presence of glucose levels in the post-pandemic period, since diabetes are among the main risk factors for severe COVID-19 symptoms [3].

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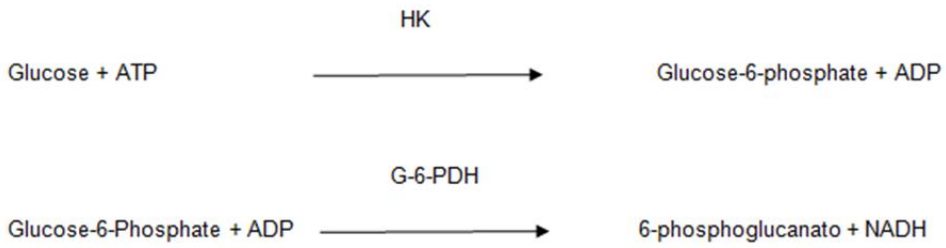
Diabetes is a known risk factor for mortality in Coronavirus disease 2019 (COVID-19) Patients [4]. SARS-CoV-2 infects peripheral blood monocytes and enhances the expression of angiotensin-converting enzyme 2 (ACE2) [5]. COVID-19 ''cytokine storm'' have been linked with higher levels of the proinflammatory cytokines as tumor necrosis factor-α (TNF-a), interleukin (IL)-1β, and IL-6 and higher levels of IFN a, b, and l expressed by monocytes infected with CoV-2 [5]. High glucose levels and glycolysis promote SARS CoV-2 (CoV-2) replication [6]. SARS-CoV-2-induced metabolic reprogramming of monocytes directly affects T cell response and lung epithelial cell death [7]. Hyperglycaemia may contribute to the development of cytokine storm by promoting proinflammatory glycosylation [4].

A systematic review and meta-analysis to analyze the impact of various comorbidities in COVID-19 had been recorded among serious events that included hypertension, Acute Respiratory Distress Syndrome (ARDS), mechanical ventilation, pneumonia, and death [8]. We conducted this study to investigate vaccinated patients against SARS-CoV-2 linked the potential of glucose levels in the post-pandemic period as predictors factors for diabetic and to document the genomics variants more recently detected in countries where people have a higher risk of develop severe illness from COVID-19.

2. Methodology

This is a retrospective epidemiology study involving patients categorized into three groups according to admission Blood Glucose (BG) levels: < 70 mg/dL; 77 – 90 mg/dL; < 99 mg/dL collected in post pandemic period among 2022 and 2023y. Patients as pregnant women and age < 18 years were excluded from this retrospective observational study conducted at All Lab. We obtained clinical and outcome data were obtained from electronic medical records of the lab. The data set was divided into normal glucose (control group), low and high glucose blood collection groups. The hexokinase enzymatic method is the reference method for determining blood glucose in serum or plasma. Sample involves the separation of the fluid part (serum) from the formed elements (red blood cells, leukocytes and other cells) and is carried out immediately, so that there is no consumption of this analyte. Adenosine triphosphate promotes the phosphorylation of glucose in a reaction catalyzed by hexokinase (HK), according to the following chemical reaction:



Hexokinase is an enzyme that catalyzes the transfer of phosphate from ATP to glucose. The chemical reaction catalyzed by the enzyme glucose 6-phosphate dehydrogenase (G-6-PDH) has high specificity for glucose 6 phosphate and therefore other hexoses or phosphorylated pentose esters do not participate in the reaction [3, 6]. Moreover, to verify the tracking of SARS-CoV-2 genomic variants, the GISAID database was used

3. Results

Normal glucose values follow reference standards between 70 and 99 mg/dL. All the results changed were confirmed by repetition sample, as reference internal quality control. Therefore, lower values are suggestive of hypoglycemia and higher values are indicative of pre-diabetes. In this study, only glucose was investigated as predictor factor to comorbidity in vaccinated patients Against SARS-CoV-2. From January 2022 to December 2022, 11.019 patients without severe COVID-19 pneumonia were documented. Of these patients, 10.004 (90.78 %) were male and 1015 (9.21%) were female. Other predictors factors to comorbidity were not analyzed as pulmonary disease, hypertension, chronic kidney disease, heart failure, and liver cirrhosis. Results are shown as means (standard deviation, SD) or medians. The samples collected from female and male investigated to glucose blood serum showed for all patients with an average proportional of 0.2264±0.3053 (CV = 0.2904) detected in the 2022 years.

About 11.019 patients who had blood glucose samples collected, 10.004 samples were male gender corresponding to 90.78% while only 1.015 samples corresponding to 9.21% female. About 11.019 patients were analyzed in 2022y, in which the most prevalent month was October with 1.425 collection visits followed by 1.177 in September for post-

pandemic glucose research. However, 89.69% had values within the expected range and 10.25% values above the expected, demonstrating a hyperglycemia index and only 0.054% hypoglycemia was detected in patients collected at the laboratory unit.

Throughout 2023y, a total of 13,246 blood samples were collected from 11,425 non-diabetic patients vaccinated against Covid-19, which 10,478 male and 947 female. Of these samples, a small portion of 11 presented between > 70mg/gL; the highest percentage was 9914 in the rate between 77 - 90 70 mg/gL and 1500 samples at the level above >90 mg/gL. Normal glucose values follow reference standards between 70- 99 mg/dL. All changed findings were confirmed by recollected sample (1.821 new samples), as reference internal quality control. Therefore, lower values are suggestive of hypoglycemia and higher values are indicative of pre-diabetes. In this study, only glucose was investigated as predictor factor to comorbidity in vaccinated patients against SARS-CoV-2. Furthermore, we detected that nondiabetic patients with good glycemic control (86.77%) and values within the expected range had high percentage rates compared with those with poorer control or values above the expected range 13.12% (Table 1 and figure 1).

In the 2022y, glucose blood samples were collected with an average proportional of 0.5± 0.79 (CV = 1.59) for values below the expected range characterized as hypoglycemia; an average proportional of 823.58±257.25 (CV = 0.31) for values within the expected range characterized as normal glucose index and an average proportional of 94.16±36.78 (CV = 0.39) for values above the expected range characterized as hyperglycemia. These findings had been demonstrated in table 1 and figure 1 below indicating the references values (Figure 2 and 3).

Table 1 Analysis of means, standard deviation and coefficient of variation of glucose blood serum collected from patients in the 2022 and 2023 years

Years	values below expected range	values within expected range	values above expected range	Patients	Samples
2022	0.5 ± 0.7977 (CV = 1.59544807)	823.5833 ± 257,2545 (CV = 0.312400482)	94.1666 ± 36.7815 (CV = 0.390940928)	918.25 ± 266.7184 (CV = 0.290463909)	1.149,25 ± 358.2965 (CV = 0.3901)
2023	0.9166 ± 1.0836 (CV = 1.182136)	826.1666 ± 138.7187 (CV = 0.167906)	125 ± 37.4918 (CV = 0.299934)	952 ± 170.8180 (CV = 0.17943)	1.104 ± 247.6408 (CV = 0.224312)

Moreover, we detected highest percentage of samples collected from men (91,71%) and lowest percentage from women (8,28%). The mean and standard deviation for the female samples were 78.9166 ± 24.3738 (CV = 0.30885), and for male were 873.1666±156.9527. Blood Glucose samples collected among female and male investigated in the 2023 year were showed in table 2.

Table 2 Analysis of means, standard deviation and coefficient of variation of glucose blood serum in patients collected in the 2022 and 2023 years

Years	Female	Male	Patients	Samples
2022	84.5833 ± 19.1523 (CV = 0.226431136)	833.6666 ± 254.5767 (CV = 0.30536998)	918.25 ± 266.71848 (CV = 0.290463909)	1149.25 ± 358.2965 (CV = 0.3117655)
2023	78.9166 ± 24.3738 (CV = 0.308855)	873.1666 ± 156.9527 (CV = 0.179751)	952 ± 170.8180 (CV = 0.17943)	1.104 ± 247.6408 (CV = 0.224312)

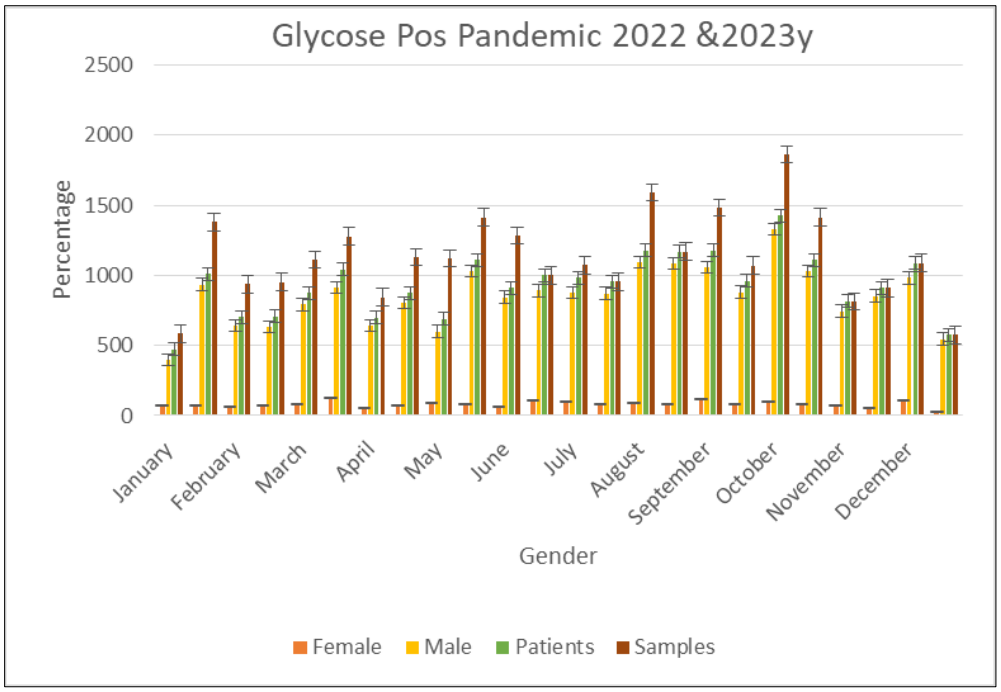


Figure 1 Reference values of glucose blood samples collected from patients in the 2022 and 2023y compared with gender

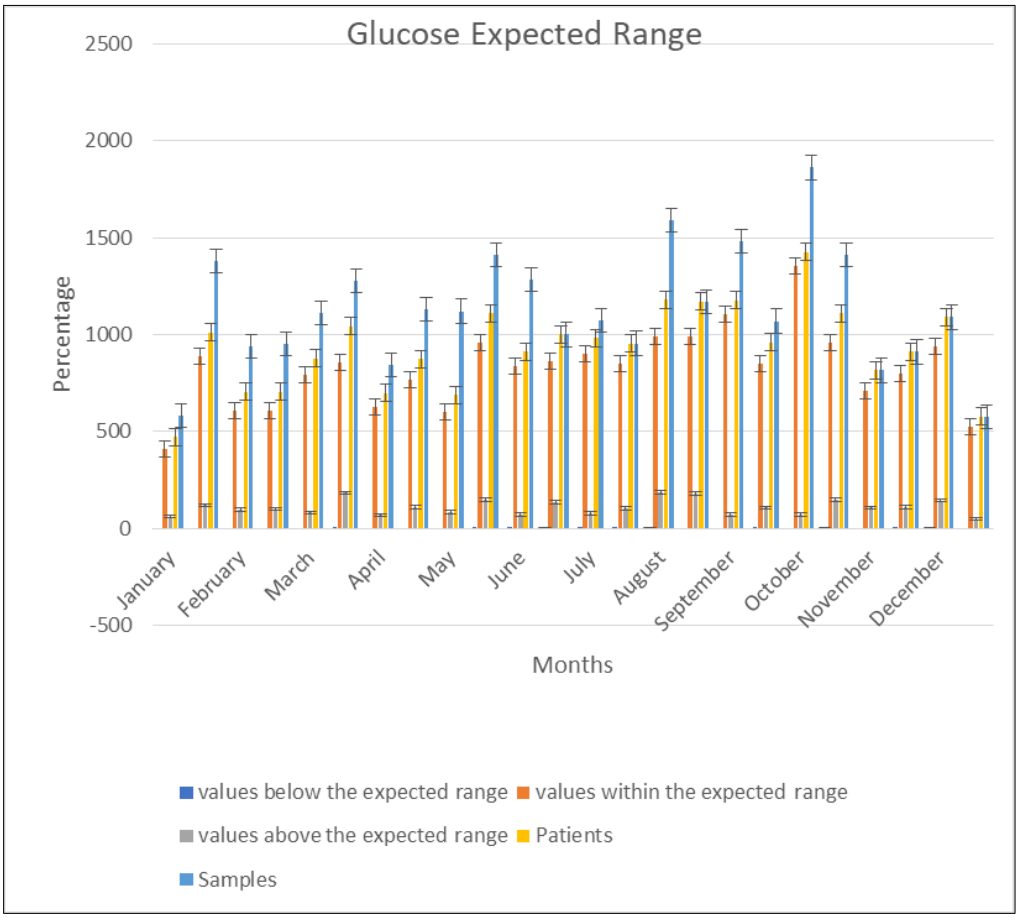


Figure 2 Reference values of glucose according the expected range from blood patients in the 2022 and 2023y

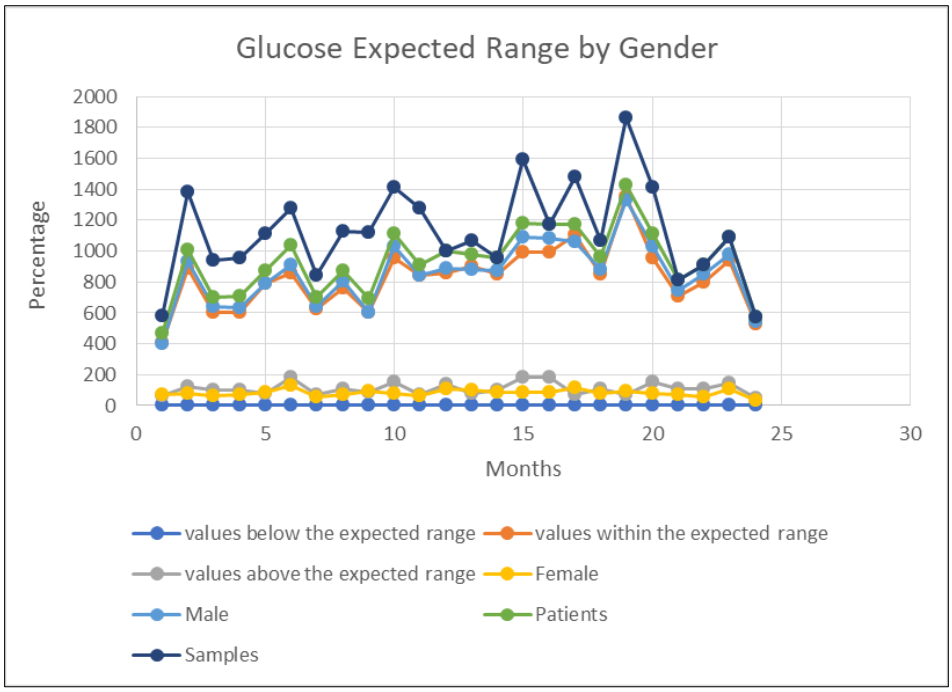


Figure 3 Reference values of glucose blood samples collected from patients in the 2022 and 2023y compared with gender

It was carried out the tracking of 19 hCoV-19 variants by accessible via GISAID EpiCoV according to the table 3 below.

Table 3 Tracking of 19 hCoV-19 genomic variants

hCoV-19 Variants	**First detected**	**Numb. of countries**	**Number of shared genomic sequences**
VOC GRA (BA.2.86+BA.2.86.*)	Denmark/Israel/USA	110	25,321
VOC GRA (XBB.1.5+XBB.1.5.*)	Austria/India/Bangladesh	152	397,222
VOC GRA (XBB.1.16+XBB.1.16.*)	India	137	131,957
VOI GRA (EG.5+EG.5.*)	Indonesia/France	114	224,642
VOI GRA (JN.1+JN.1.*)	Luxembourg/Iceland	149	511,809
VUM GRA (BA.2.75+BA.2.75.*)	India	140	128,140
VUM GRA (CH.1.1+CH.1.1*)	Austria	112	66,269
VUM GRA (XBB+XBB.* excluding XBB.1.5, XBB.1.16, XBB.1.9.1, XBB.1.9.2, XBB.2.3)	India	158	111,260
VUM GRA (XBB.1.9.1+XBB.1.9.1.*)	Indonesia/Israel/Singapore	134	103,088
VUM GRA (XBB.1.9.2+XBB1.9.2.*)	Indonesia/Egypt	114	42,272
VUM GRA (XBB.2.3+XBB.2.3.*)	India/USA	126	54,534
VOC Omicron GRA (B.1.1.529+BA.*)	Botswana/Hong Kong/South Africa	213	9,588,073
VOC Delta GK (B.1.617.2 + AY.*)	India	210	4,625,986
VOC Alpha GRY (B.1.1.7 + Q.*)	UK	191	1,212,021
VOC Gamma GR/501 Y.V3 {P.1+P.1*)	Brazil/Japan	95	137,318

VOC Beta GH/501 Y.V2 (B.1.351 + B.1.351.2+B.1.351.3)	South Africa	133	44,927
VOI Lambda GR/452 Q.V1 (C.37+C.37.1)	Peru	45	10,760
VOI Um GH (B.1.621 + B.1.621.1)	Colombia	61	16,706
VUM GH/490R (B.1.640 + B.1.640.*)	Congo/France	33	1,343

About 110 countries shared 25,321 GRA (BA.2.86+BA.2.86.*) genome sequences from sample collection to making these data publicly (http: https://gisaid.org/hcov19-variants/) – table 4.

Table 4 Most recent sample collection per country SARS-CoV-2 hCov 19 variants

Country	**Virus Name**	**Collected Data**
USA	hCoV-19/USA/CO-CDPHE-42686875/2024	2024-12-26
Poland	hCoV-19/Poland/Kce-706/2024	2024-12-13
South Africa	hCoV-19/South Africa/PATH-CERI-K064669/2024	2024-12-02
Uruguay	hCoV-19/Uruguay/DLSP_2605/2024	2024-11-29
Ukraine	hCoV-19/Ukraine/89400/2024	2024-11-27
Malaysia	hCoV-19/Malaysia/IMR_SARI-2880/2024	2024-11-24
Australia	hCoV-19/Australia/TAS008626/2024	2024-11-22
Spain	hCoV-19/Spain/AS-HUCA-232486276/2024	2024-11-20
Canada	hCoV-19/Canada/BC-BCCDC-754026/2024	2024-11-18
Russia	hCoV-19/Russia/SPE-RII-MH210283S/2024	2024-11-13
Ecuador	hCoV-19/Ecuador/NIC-INSPI-435460/2024	2024-11-12
Italy	hCoV-19/Italy/LOM_IZSLER_381503_3/2024	2024-11-05
China	hCoV-19/Heilongjiang/HLJCDC-2301/2024	2024-10-30
Chile	hCoV-19/Chile/ML-ISPC-79849/2024	2024-10-08
Czech Republic	hCoV-19/Czech Republic/NRL-s597/2024	2024-10-02
Sweden	hCoV-19/Sweden/AB-01_SE100_24CS501874/2024	2024-09-27
Germany	hCoV-19/Germany/BY-LGL-6366209/2024	2024-09-23
Mauritius	hCoV-19/Mauritius/1174930/2024	2024-09-21
Luxembourg	hCoV-19/Luxembourg/LNS0149301/2024	2024-09-16
Slovenia	hCoV-19/Slovenia/IMI-V1-9812/2024	2024-09-03
South Korea	hCoV-19/South Korea/GJ-HERI-K2482/2024	2024-09-02
Japan	hCoV-19/Japan/SUPCRC-6692/2024	2024-08-26
Netherlands	hCoV-19/Netherlands/LI-RIVM-141378/2024	2024-08-22
Philippines	hCoV-19/Philippines/PH-RITM-4723/2024	2024-08-21
Tunisia	hCoV-19/Tunisia/7999/2024	2024-08-19
Honduras	hCoV-19/Honduras/AT-325/2024	2024-08-16
Croatia	hCoV-19/Croatia/HZJZ_7866/2024	2024-08-14
Kosovo	hCoV-19/Kosovo/2059_08/2024	2024-08-09

Ireland	hCoV-19/Ireland/LK-UHL-689000/2024	2024-08-09
Brazil	hCoV-19/Brazil/AL-IB_CEVC_2401181/2024	2024-08-08
Mexico	hCoV-19/Mexico/MEX-INMEGEN-124-320/2024	2024-08-04
Ghana	hCoV-19/Ghana/FS-4400/2024	2024-08-02
Cote d'Ivoire	hCoV-19/Cote d'Ivoire/IPCI-DVE-GR3169/2024	2024-07-25
India	hCoV-19/India/MH_BJCOG_INSACOG_6871/2024	2024-07-24
United Kingdom	hCoV-19/Wales/CLIMB-CM7Y8AZP/2024	2024-07-18
Nepal	hCoV-19/Nepal/NPHL-S-2667/2024	2024-07-17
Haiti	hCoV-19/Haiti/LNSP-99170078/2024	2024-07-15
Israel	hCoV-19/Israel/ICH-741201926/2024	2024-07-13
Egypt	hCoV-19/Egypt/CPHL-EGY24349/2024	2024-07-04
Brunei	hCoV-19/Brunei/MGS-7124032185/2024	2024-07-02
Singapore	hCoV-19/Singapore/R41MQ64/2024	2024-07-02
Bahrain	hCoV-19/Bahrain/PHD-790611902/2024	2024-07-02
Uganda	hCoV-19/Uganda/C-07-017/2024	2024-06-29
Cambodia	hCoV-19/Cambodia/KCH240107/2024	2024-06-21
Denmark	hCoV-19/Denmark/DCGC-686870/2024	2024-06-17
Dominican Republic	hCoV-19/Dominican Republic/2182608-LNSPDD/2024	2024-06-15
Laos	hCoV-19/Laos/IPL-78606/2024	2024-06-13
Nigeria	hCoV-19/Nigeria/NCDC-NRL-GL-00602/2024	2024-06-06
Montenegro	hCoV-19/Montenegro/CO-01155_MNE000_1002222402/2024	2024-06-01
Colombia	hCoV-19/Colombia/ATL-INS-VG-31739/2024	2024-05-30
Botswana	hCoV-19/Botswana/R240B41_BHP_ILI-24-185/2024	2024-05-29
Taiwan	hCoV-19/Taiwan/NTU-S114/2024	2024-05-28
Switzerland	hCoV-19/Switzerland/ZH-UZH-IMV-3ba6dd9d/2024	2024-05-26
Thailand	"hCoV-19/Thailand/CU-AMV140/2024	2024-05-23
Kenya	hCoV-19/Kenya/KEMRI-2022030098/2024	2024-05-21
New Zealand	hCoV-19/New Zealand/24ZA2577/2024	2024-05-19
France	hCoV-19/France/IDF-RELAB-IPP08057/2024	2024-05-16
Portugal	hCoV-19/Portugal/PT50835/2024	2024-05-11
Puerto Rico	hCoV-19/Puerto Rico/PR-CVL-024469/2024	2024-05-10
Myanmar	hCoV-19/Myanmar/DMR_24045/2024	2024-05-07
Mozambique	hCoV-19/Mozambique/INS-PMB0700311/2024	2024-04-18
Barbados	hCoV-19/Barbados/BPH2971446/2024	2024-04-09
Austria	hCoV-19/Austria/AGES-1100790/2024	2024-03-25
Palestine	hCoV-19/Palestine/534060/2024	2024-03-19
Pakistan	hCoV-19/Pakistan/GRH42631/2024	2024-03-16
Indonesia	hCoV-19/Indonesia/JK-OUCRU-GSILab-1156421/2024	2024-03-07

Jordan	hCoV-19/Jordan/MOH-CPHL1453/2024	2024-03-04
Turkey	hCoV-19/Turkey/HSGM-AA000261/2024	2024-03-03
Greece	hCoV-19/Greece/PHLnetwork_KEDY_2440/2024	2024-03-02
Finland	hCoV-19/Finland/THL-02016/2024	2024-02-22
Romania	hCoV-19/Romania/224102/2024	2024-02-22
Norway	hCoV-19/Norway/1900/2024	2024-02-21
Belgium	hCoV-19/Belgium/Sciensano-LS-S2178/2024	2024-02-17
Slovakia	hCoV-19/Slovakia/ruvzbb-32620/2024	2024-02-16
Cyprus	hCoV-19/Cyprus/BMV11541/2024	2024-02-11
Venezuela	hCoV-19/Venezuela/Ara9502/2024	2024-02-07
Guadeloupe	hCoV-19/Guadeloupe/IPP03129/2024	2024-02-06
Hong Kong	hCoV-19/Hong Kong/HK-HKPU-PU24MB308544/2024	2024-02-05
Oman	hCoV-19/Oman/CPHL_724872/2024	2024-02-04
Lithuania	hCoV-19/Lithuania/MB240205_0070/2024	2024-02-02
Panama	hCoV-19/Panama/M272840-GMI/2024	2024-02-02
Democratic Rep. of the Congo	hCoV-19/DRC/INRB-DRC-054/2024	2024-02-01
Uzbekistan	hCoV-19/Uzbekistan/UZBRIV-303/2024	2024-02-01
North Macedonia	hCoV-19/Macedonia/IPH-MKD-578G/2024	2024-02-01
Kuwait	hCoV-19/Kuwait/Jaber20029257/2024	2024-01-31
Sint Maarten	hCoV-19/Sint Maarten/SX-RIVM-137936/2024	2024-01-29
Estonia	hCoV-19/Estonia/TLCD-34461/2024	2024-01-27
Vietnam	hCoV-19/Vietnam/NHTD-OUCRU4237/2024	2024-01-24
Cameroon	hCoV-19/Cameroon/LNSP-011-D013462/2024	2024-01-23
Guatemala	hCoV-19/Guatemala/0153-DLNS/2024	2024-01-22
Bulgaria	hCoV-19/Bulgaria/24BG_EU_024121_Pl218/2024	2024-01-22
The Bahamas	hCoV-19/Bahamas/25856-GMI/2024	2024-01-16
Grenada	hCoV-19/Grenada/184376/2024	2024-01-14
New Caledonia	hCoV-19/New Caledonia/NOU-CHT-618/2024	2024-01-09
Iceland	hCoV-19/Iceland/L-5271/2024	2024-01-08
Bolivia	hCoV-19/Bolivia/CENETROP-83/2024	2024-01-05
Argentina	hCoV-19/Argentina/HRRGL-36814358/2024	2024-01-04
Peru	hCoV-19/Peru/CAL-CITBM-CC04_05/2023	2023-12-28
Zambia	hCoV-19/Zambia/09-NIC-617/2023	2023-12-20
Hungary	hCoV-19/Hungary/100090-UPL24-000538/2023	2023-12-19
French Guiana	hCoV-19/French Guiana/GUF-IPG-1812233194/2023	2023-12-18
Madagascar	hCoV-19/Madagascar/IPM-03345/2023	2023-12-11
Costa Rica	hCoV-19/Costa Rica/INC-12153-816937/2023	2023-12-06
Lebanon	hCoV-19/Lebanon/HH-3542/2023	2023-11-26

Qatar	hCoV-19/Qatar/NIC-10-VI-0114124/2023	2023-11-19
Sri Lanka	hCoV-19/env/Srilanka/Pathogenhunters-0025-11/2023	2023-11-18
Timor-Leste	hCoV-19/env/Timor-Leste/Pathogenhunters-005-11/2023	2023-11-18
Algeria	hCoV-19/Algeria/12399/2023	2023-11-06
Morocco	hCoV-19/Morocco/INH_UM6P-1106/2023	2023-07-02

4. Discussion

It has been demonstrated that hyperglycemia in patients with COVID-19 is associated with a higher risk of mortality. So, our study focused on the possibility of vaccinated patients against COVID-19 showed controlled glucose blood levels. This is a retrospective epidemiology study involving patients categorized into three groups according to admission Blood Glucose (BG) levels: < 70 mg/dL; 77 – 90 mg/dL; < 99 mg/dL collected in 2022 and 2023y. Therefore, lower values are suggestive of hypoglycemia and higher values are indicative of pre-diabetes. According to Nandy et al., 2020, the presence of Diabetes mellitus (DM) has a significant impact on mortality rate in COVID-19 patients. Some studies have demonstrated that COVID-19 affects endocrine system causing glucose dysregulation mainly in approximately 50% of those who are hospitalized with COVID-19 [7, 8, 9]. And the emergence and reemergence of viral diseases may be accompanied by the genomic and epidemiology surveillance to mitigate any risk of propagation of the novel possible variant viral [10,11]. Concerning our results, glycemic testing should be recommended since high glucose levels were associated with COVID-19 patients [6;7].

5. Conclusion

Our study dataset was a backward-looking study which the glucose parameter listed in the electronic medical records could be analyzed as focuses the predictor factor in vaccinated patients against SARS-CoV-2. Therefore, we decide not to include the whole values of the machine learning model. In this study population, we concluded that new insulin therapy could be applied in future studies including diabetic patients vaccinated against COVID-19. It is also added that comorbidities were not considered in the analysis of controlled glucose levels and/or considered within the normal reference standard. Therefore, further studies are needed to better be understanding of measurement in diabetic patients at high risk for COVID-19. New insulin therapy or increased dosing from baseline had not been considered. So, as a perspective for the next steps, the authors intend to investigate positive cases of SARS-CoV-2 and identify the circulating genomic variant related to the increase in glucose levels. Genomic tools as Next Generation Sequencing (NGS) for the characterization of viral samples and in genetic engineering for the development of vaccines had been advanced molecular studies during SARS-CoV-2 pandemic.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that they have no conflict of interest.

Statement of ethical approval

Ethical clearance was obtained from the ethical review committee of Department of Sciences Medicine University in accordance with ethical principles for the guidance of physicians in medical research.

All research was performed in accordance with the relevant guidelines and regulations. Data was accessed from January, 2022, to December, 2023, and access to the collected information was limited to the principal investigator and confidentiality was maintained throughout the project.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

Role of the funding source

There was no funding source for this study.

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