Original Article

Study of HbA1c levels in non-diabetic individuals recovered from Covid-19

Sainithesh Gandikota[1], Kothapalle Sowmya Sudha[2], Madhavi Latha Naramalli[3]

[1]Department of Medicine, Sri Venkateswara Ramnarayan Ruia Government General Hospital, Sri Venkateshwara Medical College, Tirupati, Andhra Pradesh, India, [2]Department of Community Medicine, ACSR Government Medical College, Nellore, Andhra Pradesh, India, [3]Department of Bio Chemistry, Sri Venkateshwara Medical College, Tirupati, Andhra Pradesh, India

Abstract

Objectives: To study the glycemic control by estimating HbA1c levels among previously non-diabetic individuals aged above 40 years, who recovered from coronavirus disease 2019 (Covid-19) infection. **Materials and Methods:** This is an analytical cross-sectional study of people affected with Covid-19 infection, who were home-isolated, hospitalized, and discharged. The simple random sampling technique was used for the study group. Tirupati City, Andhra Pradesh State, India. We assessed socio-demographic profiles, hba1c levels, RBS, and severity of infection. The obtained laboratory reports were analyzed by using means and proportions after entering data in MS Excel and converted to SPSS software new version. **Results:** The study participants comprised mostly middle age group males and females (mostly 40–60 years, with 60% of them being females). Most of the study subjects were healthy, and 58% of them have normal hba1c levels. 32% of them are in border line diabetic. The prevalence of diabetes post Covid-19 infection is 10%. The majority of participants have normal random blood sugar levels (around 92%), and very less individuals have abnormal random blood sugar levels (2% of the subjects). There is no significant association between hypertension and raised blood sugar levels post Covid-19 infection. **Conclusions:** Based on the study, Covid-19 infection has an impact on blood sugar levels and altered glycemic control, switching a few individuals into diabetic and a significant number of individuals into the pre-diabetic state, who are non-diabetic individuals before Covid-19 infection.

Keywords: Covid-19, diabetes, HbA1c, post-Covid recovery, RBS

Introduction

The novel severe acute respiratory syndrome coronavirus (SARS-CoV-2), which just appeared as coronavirus disease 2019 (Covid-19), is a contagious illness. SARS-CoV-2 is distinct from earlier coronavirus infections (SARS and Middle-East respiratory syndrome) because of its high infectivity (reproduction value, r0, often 2-4), pre- or asymptomatic transmission, and other characteristics that have aided in the current global Covid-19 epidemic. Age, male sex, diabetes, obesity, and hypertension are all known risk factors for the severity of the illness and death caused by SARS-CoV-2 infection. The causes of these connections are still mostly unknown. Evidence is also mounting, suggesting that the underlying pathophysiology of hyperglycemia in diabetics is made worse by SARS-CoV-2 infection.[1]

SARS has been linked to a number of processes, including immune-mediated beta-cell destruction and directly virus-induced beta cell death. Angiotensin-converting enzyme-2 (ace-2) receptors are a common entry route for corona virus 2 (SARS-CoV-2) and favor involvement of

Address for correspondence: Dr. Sainithesh Gandikota, Sri Venkateshwara Medical College, Tirupati - 517 501, Andhra Pradesh, India.
E-mail: gandikotasainithesh@gmail.com

Received: 13-04-2023 **Revised:** 13-06-2023
Accepted: 15-06-2023 **Published:** 21-11-2023

Access this article online

Quick Response Code:

Website: http://journals.lww.com/JFMPC

DOI: 10.4103/jfmpc.jfmpc_639_23

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Gandikota S, Sowmya Sudha K, Naramalli ML. Study of HbA1c levels in non-diabetic individuals recovered from Covid-19. J Family Med Prim Care 2023;12:2727-32.

multiple organs.[2] Affected systems include the heart, digestive system, central nervous system, and coagulation cascade. There are not many reports of endocrine involvement.[3,4] In Covid-19,[5] hyperglycemia is frequently noted. Using organoid derivatives derived from human pluripotent stem cells, a recent study that investigated the physiological model for SARS-CoV-2 showed alpha- and beta-cell death brought on by viral cytotoxic effects.[6] Acute diabetes and hyperglycemia are the outcomes of islet cell damage caused by SARS-CoV-2. Hyperglycemia can also occur when patients with severe Covid-19 are treated with glucocorticoids.[7] Finally, changes in glucose metabolism brought on by a stress reaction may cause hyperglycemia.[8]

Corticosteroids have negative direct effects on insulin secretion and cause insulin resistance in the liver, adipocytes, and skeletal muscle. The pathogenesis of corticosteroid-induced diabetes is heavily influenced by the development of insulin resistance during corticosteroid therapy and the inadequate adaptation of insulin secretion.[9] In this study, non-diabetic persons who have recovered from Covid-19 will be examined for the impact of Covid on glycemic control as measured by HbA1c levels.

Materials and Methods

- Study design: Analytical cross-sectional study.
- Study subjects: 500 individuals recovered from Covid-19.
- Inclusion criteria
  1) Individuals with no history of diabetes mellitus.
  2) Individuals should be recovered from Covid-19 (a minimum recovery period of 3 months).
  3) Individuals of an age group above 40 years.
  4) Mild (or) moderately (or) severely affected with Covid-19 in the past.
- Exclusion criteria
  1) Age <40 years
  2) h/o diabetes mellitus
  3) h/o of anemia
  4) Individuals not willing to participate in the study.
- **Sampling technique:** The simple random sampling technique was used for the study group.
- **Study method:** HbA1c levels are estimated from 2 ml ethylenediaminetetraacetic acid blood sample with informed consent according to the instructions provided in the kit provided by the manufacturer, and the method used is turbidometry.
- **Consent:** Written consent was taken by the principal investigator from each and every individual after giving adequate information.

Results

From the study, the age group of the study participants ranges from 40 to 72 years, the mean age of the study participants is 48.9 years, and the standard deviation (SD) is 7.3 years.

From Figure 1, the majority of the study participants were in the age group of 40–45 years, about 36%, followed by 46–50 years group, about 24% of the subjects.

Figure 2 shows the gender-wise distribution of the study participants; 20% of them are males, and 60% are females.

The HbA1c levels of study subjects range from 3.1% to 8.6%, and the mean HbA1c level is 5.5% with a standard deviation of 0.8%, with a 95% confidence interval of 5.55 ± 0.072. The majority of the subjects, around 52%, fall in the range of 4.5–5.5% HbA1c level, followed by 5.5–6.5% range, who are around 32% as shown in Figure 3.

The random blood sugar levels of study subjects range from 42.27 mg/dl to 200.12 mg/dl, and the mean random blood sugar level is 112.81 mg/dl with a standard deviation of 23.28, with a 95% confidence interval of 112.81 ± 2.07. The majority of the subjects, around 92%, fall in the level <150 mg/dl random blood sugar level, followed by 150 mg/dl to 200 mg/dl range, who are around 6%, as shown in Figure 4.

The severity criteria used for this study, according to World Health Organization severity definitions, are

- Critical Covid-19: Defined by the criteria for acute respiratory distress syndrome (ARDS), sepsis, septic shock, or other conditions that would normally require the provision of life-sustaining therapies such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy.
- Severe Covid-19: Defined by any of the following:

Oxygen saturation <90% on room air, respiratory rate >30 breaths/min in adults and children >5 years old, e60 breaths/min in children <2 months old, ≥50 in children 2–11 months old, and ≥40 in children 1–5 years old.

Signs of severe respiratory distress (accessory muscle use, inability to complete full sentences, and, in children, very severe chest wall indrawing, grunting, central cyanosis, or the presence of any other general danger signs).

- Non-severe Covid-19: Defined as the absence of any criteria for severe or critical Covid-19.

In the study, the majority of the participants were mildly infected, around 46%, followed by severely affected individuals, around 36%, as shown in Figure 5.

The post recovery period of the study subjects ranges from 3 months to 9 months, with a mean post recovery period of 4.9 months, a standard deviation of 1.81, and a 95% confidence interval of 4.96 ± 0.161. 63% of the study respondents belong to 3–5 months of post recovery period, as shown in Figure 6.

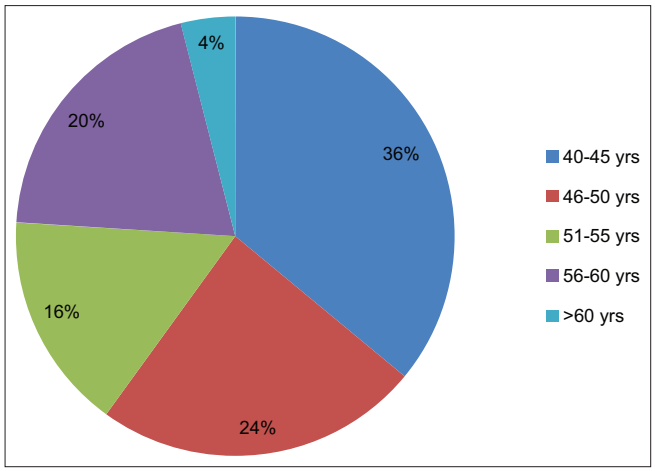

Figure 1: Age distribution in study participants

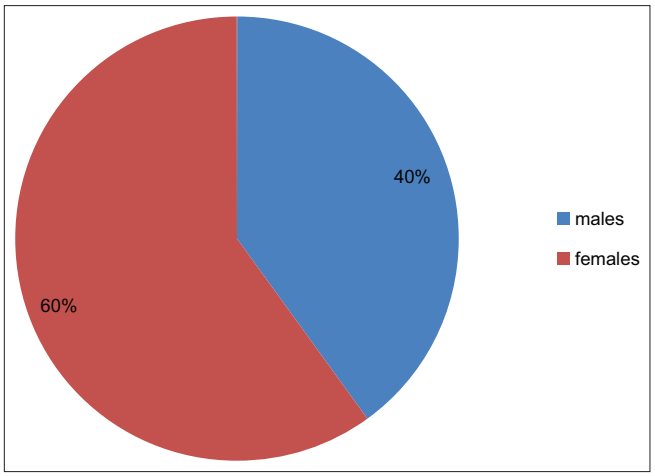

Figure 2: Gender distribution in study participants

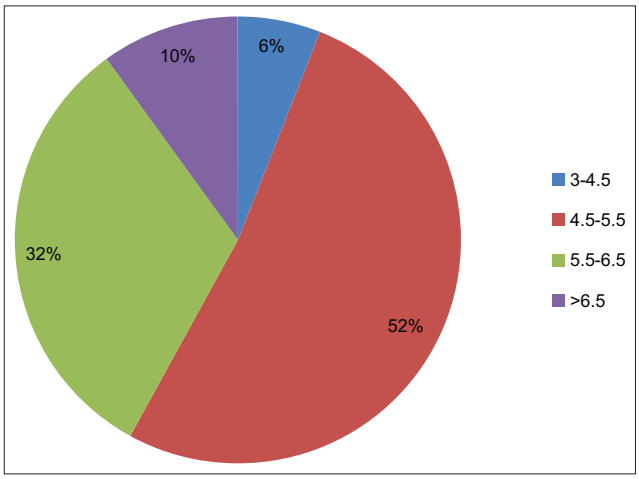

Figure 3: HbA1c levels distribution in study participants

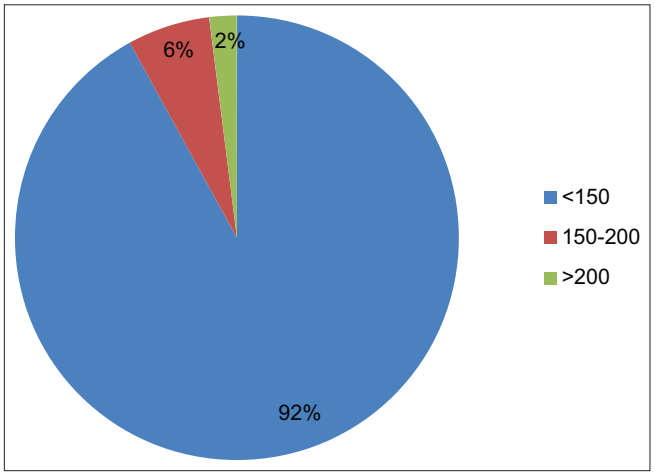

Figure 4: Random blood glucose distribution in study participants

From Figure 7, we can see the HbA1c levels in different age groups, and the study shows that 10% of the study subjects were diabetic and 4% of them belong to the 40–45 years age category. Around 52% of the study participants have HbA1c levels in the 4.5–5.5% range. *P* value <0.0001.

Figure 8 gives a clear picture about random blood glucose levels, and 92% of the population have <150 mg/dl and the majority of them are in the middle age group, that is, 40 years to 60 years. The *P* value is 0.0004.

The association between HbA1c levels and severity of the Covid infection is depicted in Figure 9, and the study shows that 46% were in the mild grade, with 26% of them having 4.5–5.5% HbA1c levels. The *P* value is 0.0048.

Figure 10 shows the comparison between HbA1c levels and the post recovery period from Covid-19 infection. The majority of the subjects, about 46%, participated in the study with a post recovery period of 3–5 months, and 6% of them had HbA1c levels >6.5%. *P* value <0.0001.

Discussion

Primary and community health care providers, family physicians, and community nurses have a great role in health educating the population. They need to know and be aware of the relation between diabetes or pre-diabetic state and Covid-19 infection, in regard to the future outcome of the individual health at the primary or community level, and make necessary and innovative steps and possible approaches in understanding and improving public health.

Study population

The study participants comprised mainly middle-age group individuals with 40 years as the lower limit for the study and with no upper limit. Individuals above 40 years in this study are assessed by checking previous values of their blood sugar levels (fasting blood sugars and post-prandial blood sugars) and are identified as non-diabetic individuals before conduct of study. The subjects who participated in the study are with normal hemoglobin levels and with no anemia or hemoglobinopathies as the study is by estimation of HbA1c levels. Individuals with

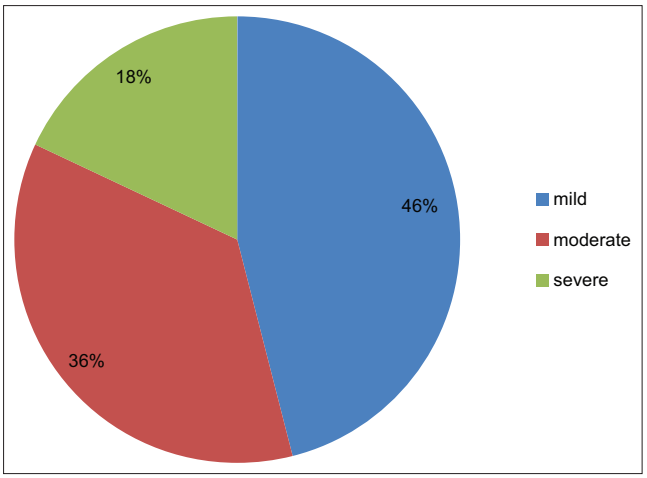

Figure 5: Severity distribution in study participants

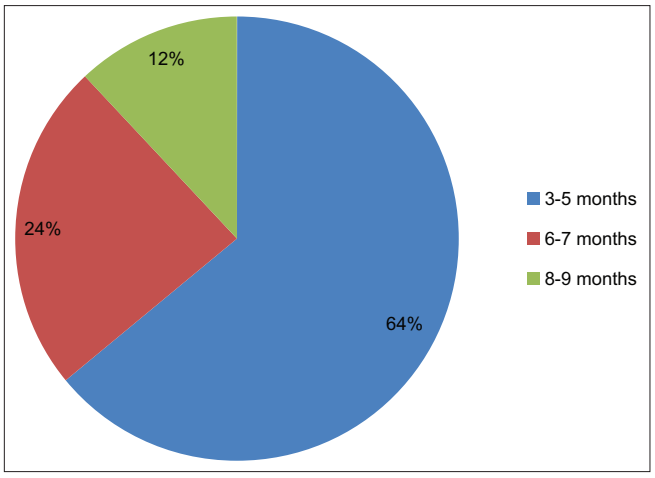

Figure 6: Post recovery period in study participants

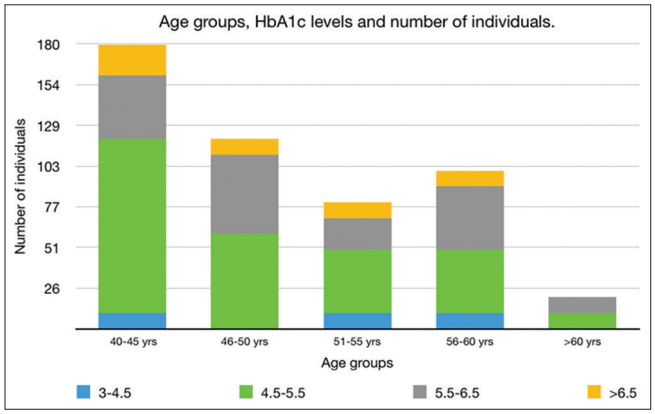

Figure 7: Comparison of age and HbA1c levels

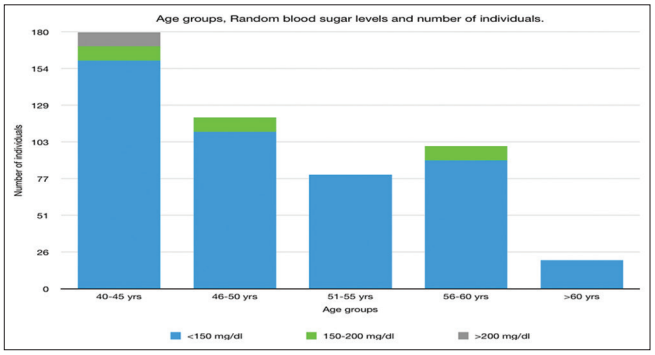

Figure 8: Comparison of age and random blood sugar levels

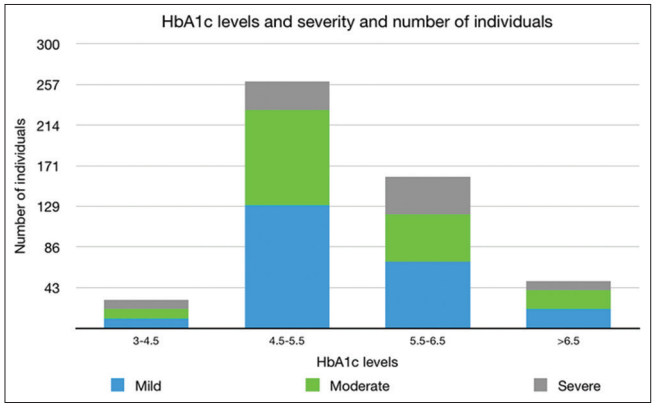

Figure 9: Comparison of HbA1c levels and severity

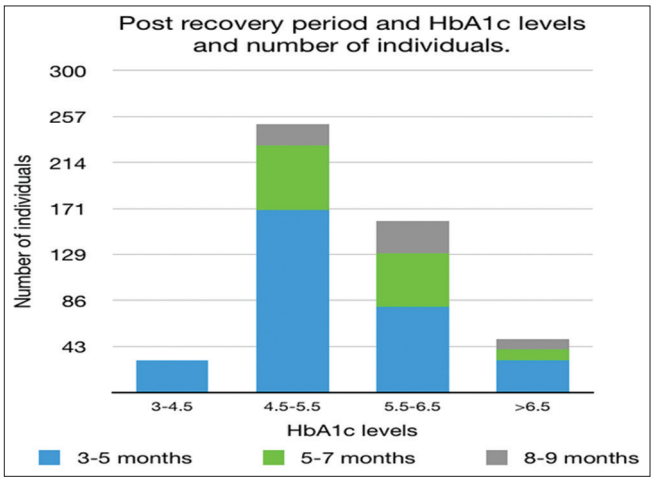

Figure 10: Comparison of HbA1c levels and post recovery period

asymptomatic Covid-19 infection are not considered and did not participate as it has no significance in the study.

Significance of the post recovery period in the study

The minimum post recovery period for the study is 3 months, that is, 3 months from the date of negative reverse transcriptase polymerase chain reaction Covid test, and there is no upper limit for the post recovery period. The significance of 3 months of minimum post recovery period is to rule out the Covid infection-induced hyperglycemia at the stage of active infection and hyperglycemia induced by therapeutic agents as in the case of corticosteroid therapy in patients with severe Covid infection, that is, admitted in the intensive care unit for treatment and recovery. The corticosteroids used in the treatment for Covid infection elevate the blood glucose levels by opposing the insulin action and stimulate gluconeogenesis, especially in the liver, resulting in a net increase in the hepatic glucose output.

Table 1: Severity distribution of post covid diabetics

Severity of infection	Non-severe	Severe	Critical	Total
Post-Covid diabetics	4%	4%	2%	10%

Table 2: Age distribution of post covid diabetics

Age group	40-50 years	50-60 years	Total
Post-Covid diabetics	6%	4%	10%

These elevated blood sugar levels due to Covid infection and corticosteroid therapy (in some individuals with moderate to severe infection) reflect on the HbA1c levels. As HbA1c, that is, glycosylated hemoglobin, shows the blood sugar levels for the past 2–3 months, there will be raised HbA1c levels if tested within 3 months of the Covid-19 infection. Hence, to rule out the infection and therapy-induced hyperglycemia as it masks the pathophysiology of pancreas, individuals are selected with a minimum post recovery period of 3 months.

Association between HbA1c levels, random blood glucose levels, and Covid-19 infection

In the present study, 32% of them turned into borderline diabetic by considering their HbA1c levels, and 10% of study participants had HbA1c levels elevated compared to normal (even after 3 months of post-recovery period). Among 10% of post-Covid diabetic individuals, it was found that 4% of them had mild infection, 4% of them had severe infection, and 2% of them had critical Covid infection [Table 1].

Among 10% of post-Covid diabetic individuals, it was found that 6% of them belong to age group of 40–50 years and 4% of them belong to the age group of 50–60 years [Table 2].

Random blood glucose sugars are high only in 2% of study subjects, and those 2% belong to the age group of 40–45 years.

There are only 20% of known hypertensives, and 2% of them have turned post-Covid diabetic, which is not significant.

Among 10% of new post-Covid diabetics, 6% of them turned diabetic within 3–5 months of post recovery period, 2% of them within 6–7 months, and 2% of them within 8–9 months of post recovery period.

Conclusions and Summary

i. Covid-19 infection has an impact on blood sugar levels and altered glycemic control, switching a few individuals into diabetic and a significant number of individuals into the pre-diabetic state, who are non-diabetic individuals before Covid-19 infection.
ii. The study participants comprised mostly middle age group males and females (mostly in 40–60 years, with 60% of them being females).
iii. Most of the study subjects were healthy, and 58% of them have normal HbA1c levels. 32% of them are border line diabetic.
iv. The prevalence of diabetes post Covid-19 infection is 10%.
v. The majority of participants have normal random blood sugar levels (around 92%), and very less individuals have abnormal random blood sugar levels (2% of the subjects).
vi. There is no significant association between hypertension and raised blood sugar levels post Covid-19 infection.

Recommendations

The key take home points:

i. With this study, we recommend to maintain strict HbA1c levels and random blood sugars to prevent a further post-Covid diabetic status. Primary health care providers have a great role in health educating the population.
ii. Regular periodic checking of HbA1c levels and random blood glucose levels is recommended for further 2 years of post-Covid recovery for the Covid-infected individuals at their nearest primary or community health center.
iii. Complete to partial removal of stress (because stress exaggerates diabetes) and lifestyle modifications have to be done and are encouraged by family physicians and community health providers.
iv. Promotion of yoga, meditation, walking, and an increase in physical activity has to be done.
v. Strict glycemic control is to be monitored and maintained during and after Covid-19 infection.
vi. Primary care providers should make a follow-up on the post-Covid recovery individuals, make records, initially in assessing and providing better health to decrease the morbidity, and make an impact at community health.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Muniangi-Muhitu H, Akalestou E, Salem V, Misra S, Oliver NS, Rutter GA. Covid-19 and diabetes: A complex bidirectional relationship. Front Endocrinol (Lausanne) 2020;11:582936. doi: 10.3389/fendo.2020.582936.
2. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 2004;203:631-7. doi: 10.1002/path.1570.
3. Tan T, Khoo B, Mills EG, Phylactou M, Patel B, Eng PC, *et al.* Association between high serum total cortisol concentrations and mortality from COVID-19. Lancet Diabetes Endocrinol 2020;8:659-60. doi: 10.1016/S2213-8587(20)30216-3.
4. Wang W, Su X, Ding Y, Fan W, Zhou W, Su J, *et al.* Thyroid function abnormalities in COVID-19 patients. Front

Endocrinol (Lausanne) 2021;11:623792. doi: 10.3389/fendo.2020.623792.

5. Iacobellis G, Penaherrera CA, Bermudez LE, Bernal Mizrachi E. Admission hyperglycemia and radiological findings of SARS-CoV2 in patients with and without diabetes. Diabetes Res Clin Pract 2020;164:108185. doi: 10.1016/j.diabres.2020.108185.
6. Yang L, Han Y, Nilsson-Payant BE, Gupta V, Wang P, Duan X, *et al.* A Human pluripotent stem cell-based platform to study SARS-CoV-2 tropism and model virus infection in human cells and organoids. Cell Stem Cell 2020;27:125-36. doi: 10.1016/j.stem.2020.06.015.
7. Kwon S, Hermayer KL, Hermayer K. Glucocorticoid-induced hyperglycemia. Am J Med Sci 2013;345:274-7. doi: 10.1097/MAJ.0b013e31828a6a01.
8. Chinsky K. The evolving paradigm of hyperglycemia and critical illness. Chest 2004;126:674-6. doi: 10.1378/chest.126.3.674.
9. Bastin M, Andreelli F. [Corticosteroid-induced diabetes: Novelties in pathophysiology and management]. Rev Med Interne 2020;41:607-16. doi: 10.1016/j.revmed.2020.05.007.