COVID-19 Effects on Glycemic Control in Diabetics Compared to Healthy Individuals

Zahra Moradi[1], Mostafa Tohidian[1], Zahra Movahednia[2], Fatemeh Mahmoudikohani[3], Susan Samimi[4], Mostafa Moazamfard[2], Sheida Jamalnia[5], Hamid Behrouj[6*]

1- Doctor of pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

2- Department of Operating Room, Faculty of Paramedicine, Behbahan University of Medical Sciences, Behbahan, Iran.

3- Department of Midwifery, School of Nursing and Midwifery, Bam University of Medical Sciences, Bam, Iran.

4- Department of Health Information Technology, School of Allied Medical Sciences, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

5- Medical Journalism Department, Shiraz University of Medical, Shiraz, Iran.

6- Behbahan Faculty of Medical Sciences, Behbahan, Iran.

Corresponding author: Hamid Behrouj,Behbahan Faculty of Medical Sciences, Behbahan,Iran. Email: h.behrooj68@gmail.com, Mobile: +989380078603

Author contribution: Zahra Moradi, Mostafa Tohidian, and Hamid Behrouj assisted with the design of the study and participated in most of the experiments. Zahra Movahednia, Fatemeh Mahmoudikohani, and Susan Samimi carried out the design and coordinated the study, participated in most of the experiments, and data analysis. Mostafa Moazamfard, and SheidaJamalnia participated in sample collection, data gathering, manuscript preparation, and correction.

Place of work: The Behbahan University of Medical Sciences (Behbahan, Iran).

Abstract

Background: numerous studies have reported that COVID-19 can affect various organs and tissues in the body, including the pancreas. This study aimed to evaluate the effect of COVID-19 on fasting blood glucose, hemoglobin A1c, and insulin in COVID-19 infected patients. **Methods:** Three hundred patients with positive SARS-CoV-2 real-time PCR tests were included in the study. Based on their fasting blood glucose and hemoglobin A1c status they were divided into normoglycemic, prediabetic, and diabetic groups. Fasting blood glucose, hemoglobin A1c, and fasting insulin levels were measured during and three months after COVID-19 infection. **Results:** there were no statistically significant differences between fasting blood glucose, hemoglobin A1c, and fasting insulin levels during and three months after COVID-19 infection between all study groups. **Conclusion:**despite conflicting previous reports, the present study results suggest that COVID-19 infection can not interfere with glycemic control and related markers.

Keywords: Fasting Blood Glucose; Hemoglobin A1c; Insulin; COVID-19; Diabetes

1. Introduction

COVID-19 pandemic now poses huge health problems around the world[1-4]. Although initially thought to be a respiratory disease, several studies have shown that it can affect various organs and tissues in the body, including the digestive system, cardiovascular system, liver,

ovaries, brain, and pancreas[5-7]. Direct attack by theSARS-CoV-2 through ACE2 receptor, severe inflammatory response syndrome, ischemia-reperfusion injury, underlying diseases, and drug-induced injury are enumerated as potential etiologic factors for tissue injury in COVID-19[8-10].

The relationship between COVID-19 infection and diabetes has been shown in previous studies. Covid 19 causes more severe disease, hospitalization, and death in diabetics than in healthy people. It is found that the hospitalization rate of COVID-19 infected diabetics is22%, but the same number in the total population is about 10% [11, 12]. Another study found that the mortality rate of diabetics was two-fold higher than the normal population[13, 14]. One reason for this could be a change in ACE2 receptor expression in diabetic people's tissues[15].

High blood glucose can facilitate the virus replication in the lung cells and prevent the proper immune system response [16, 17]. Recent studies have shown that during and after Covid-19 infection glycemic control has decreased and insulin use has increased in many cases. Guo W *et al.*'s study on COVID-19 infected diabetic patients reported that 29% of patients were treated with insulin before infection, while after the disease this reached 37% [18].

Due to the Covid-19 destructive effects on pancreatic tissue and the direct relationship between blood glucose control and disease severity, hospitalization, and mortality, this study aimed to evaluate the effect of Covid 19 on fasting blood glucose, hemoglobin A1c, and insulin in COVID-19 infected patients.

2. Materials and Methods

2.1. Study design

Three hundred patients with positive SARS-CoV-2 real-time PCR tests were included in the study. Patients were selected based on their fasting blood glucose and hemoglobin A1c status and divided into three groups: (A) 100 normoglycemic individuals, (B) 100 prediabetic patients, and (C) 100 diabetic patients. Normoglycemia was defined as fasting blood glucose lower than 100 mg/dl and Hb A1c less than 5.7%. Prediabetes was defined as fasting blood glucose between 100 and 125 mg/dl and Hb A1c between 5.7 and 6.4%. Diabetes was defined as fasting blood glucose higher than 125mg/dl and Hb A1c higher than 6.4%. All patients signed a written consent form before participating in the study. The ethics committee of Behbahan University of Medical Sciences approved the study (IR.BHN.REC.1400.028). All patients were tested for fasting blood glucose, hemoglobin A1c, and insulin at the onset of Covid-19 and three months later. The inclusion criteria were: male and female patients, age minimum 18 and maximum 80 years, and no underlying diseases other than diabetes. The exclusion criteria were Age under 18 years and over 80 years, the presence of underlying diseases including cardiovascular diseases, metabolic disorders, neurological diseases, hypertension, kidney diseases, and liver diseases.

2.2. Measurements

Blood glucose was measured using the Biorexfars Glucose assay kit (Biorexfars co, Shiraz, Iran). Hb A1c was measured using Diazym direct enzymatic assay kit (Diazyme Laboratories, Inc., Poway, California). Fasting insulin was measured using a Human Insulin ELISA Kit (Abcam co., UK). A Mindray BS200 autoanalyzer (Shenzhen, China) and a Statfax 3200 ELISA reader (Westport, Connecticut, USA) were used for assays.

Statistical analysis

Data are presented as mean ± standard error of mean (M±SEM). To determine the normality of data, the Kolmogorov–Smirnov test was used. The differences between groups were analyzed using Kruskal-Wallis with post-hoc Mann-Whitney U test. SPSS software (version 25.0 for Windows) was used for statistical analyses. $P<0.05$ was considered as statistically significant.

3. Results

Baseline characteristics of the study population are shown in Table 1. Fasting blood glucose and Hb A1c were slightly higher after three months of COVID-19 infection in all groups, however, the differences were not statistically significant. There was no significant difference between FBS, A1c, and Ins in all groups. Ins level was higher in prediabetic patients than in the normoglycemic group. In diabetic patients, the mean Ins level was lower than the normoglycemic group.

Table 1. Baseline characteristics of the study population were stratified by groups.

Variables		Groups			P value
		Normoglycemic (N=100)	Prediabetic (N=100)	Diabetic (N=99[√])	
Age (Y)		53±8	56±12	57±13	0.13
Sex	Male	57	51	54	0.21
	Female	43	49	46	
BMI	Normal	71	68	64	**0.04***
	Overweight	18	19	22	
	Obesity	11	13	16	
Smoking	Current	21	10	15	0.32
	Former	10	6	14	
	Never	69	74	71	

*Significantly different.

[√] A diabeticparticipant died during the study.

Table 2.FBS and HbA1c values during and after COVID-19 infection in normoglycemic, prediabetic, and diabetic patients.

	FBS (mg/dl)		
	Before	**After**	**P**
Normoglycemic	87±19	91±24	0.42
Prediabetes	117±8	119±11	0.25
Diabetes	155±48	168±58	0.34
	Hb A1c (%)		
	Before	**After**	**P**

Normoglycemic	4.9±1.1	5±0.9	0.45
Prediabetes	5.4±1.5	5.5±1.3	0.21
Diabetes	7.7±2.9	8.1±3.2	0.13

Data are shown as Mean±SEM. P<0.05 was considered statistically significant.

Table 3.Ins values during and after COVID-19 infection in normoglycemic, prediabetic, and diabetic patients

	Ins (mIU/L)		
	Before	**After**	**P**
Normoglycemic	17±3	16±4	0.11
Prediabetes	27±6	26±8	0.36
Diabetes	11±5	12±6	0.24

Data are shown as Mean±SEM. P<0.05 was considered statistically significant.

4. Discussion

The present study was designed to investigate the impact of COVID-19 on FBS, Hb A1c, and Ins. These markers were assessed during and three months after infection in normoglycemic, prediabetic, and diabetic patients. Our results suggest that COVID-19 can not interfere with glycemic control in all studied groups.

Whether the alterations of glucose metabolism that occur with a sudden onset in severe COVID-19 persist or remit when the infection resolves is unclear [11]. We could not find any prospective study which reports diabetic-related markers after COVID-19 infection. An international group of leading diabetes researchers is establishing a Global Registry of COVID-19-related diabetes. This registry is specifically designed to establish the extent and characteristics of new-onset, COVID-19-related diabetes, and to investigate its pathogenesis, management and outcomes. The Registry also collects data about presentations with severe metabolic disturbance in pre-existing diabetes. However, no reports are available regarding the registry collected data. Results of the present study showed that COVID-19 did not affect FBS, Hb A1c, and Ins in three months. If we conclude based on these results, it seems that we should not worry about the blood glucose regulation after COVID-19 infection even in diabetic patients. However, several recent studies on the effects of COVID-19 on the pancreas report that SARS-CoV-2 can cause pancreatic involvement, thereby disrupting the natural mechanism for controlling blood glucose. A threefold increase in pancreatic amylase and lipase enzymes in COVID-19 infected patients proves this [19].Pathological studies of pancreatic tissue have also shown abnormalities such as fibrosis, thrombosis, and endothelialitis in the pancreatic tissue of COVID-19 infected patients. Impaired insulin secretion and decreased number of insulin-secreting beta cells have also been reported in these patients [20]. Numerous mechanisms for pancreatic damage have been reported during COVID-19, including direct virus attack to the beta cells, severe inflammatory response to

disease, ischemic-reperfusion injury, as well as exacerbation of endocrine underlying diseases due to COVID-19 [21, 22].

Although these studies report conflicting data, all of them have investigated the worse effects of SARS-CoV-2 on the pancreas during COVID-19 infection. More studies should be performed to clarify the exact effects of COVID-19 on glycemic control and glucose metabolism. The present study had some limitations. The sample size was low and other related metabolic factors such as lipid profile were not assessed.

Conclusion

Despite conflicting previous reports, the present study results suggest that COVID-19 infection can not interfere with glycemic control and related markers including FBS, Hb A1c, and Ins.

Acknowledgment

This work was supported by grants from Behbahan University of Medical Sciences. The authors appreciate the support of the dissertation grant.

Funding

This work was supported by grants from Behbahan University of Medical Sciences (Grant No:400038).

Conflict of interests

The authors declare that there are no conflicts of interest.

References

[1]. Vakili S, Akbari H, Jamalnia S. Clinical and Laboratory findings on the differences between h1n1 influenza and coronavirus disease-2019 (covid-19): focusing on the treatment approach. Clinical Pulmonary Medicine. 2020;27(4):87-93.

[2]. Li D, Ding X, Xie M, Tian D, Xia L. COVID-19-associated liver injury: from bedside to bench. Journal of Gastroenterology. 2021;56(3):218-30.

[3]. Kadhom M, Al-Doori AN, Ahmed DS, Yousif E. Herbal medicine as an alternative method to treat and prevent COVID-19. Baghdad Journal of Biochemistry and Applied Biological Sciences. 2021;2(01):1-20.

[4]. Weaver RH, Jackson A, Lanigan J, Power TG, Anderson A, Cox AE et al. Health behaviors at the onset of the COVID-19 pandemic. American journal of health behavior. 2021;45(1):44-61.

[5]. Vakili S, Savardashtaki A, Jamalnia S, Tabrizi R, Nematollahi MH, Jafarinia M et al. Laboratory findings of COVID-19 infection are conflicting in different age groups and pregnant women: a literature review. Archives of medical research. 2020;51(7):603-7.

[6]. Adeghate EA, Eid N, Singh J. Mechanisms of COVID-19-induced heart failure: a short review. Heart Failure Reviews. 2021;26(2):363-9.

[7]. Massabeti R, Cipriani MS, Valenti I. Covid-19: A systemic disease treated with a wide-ranging approach: A case report. Journal of Population Therapeutics and Clinical Pharmacology. 2020;27(SP1):e26-e30.

[8]. Gavriatopoulou M, Korompoki E, Fotiou D, Ntanasis-Stathopoulos I, Psaltopoulou T, Kastritis E et al. Organ-specific manifestations of COVID-19 infection. Clinical and experimental medicine. 2020;20(4):493-506.
[9]. Dorward DA, Russell CD, Um IH, Elshani M, Armstrong SD, Penrice-Randal R et al. Tissue-specific immunopathology in fatal COVID-19. American journal of respiratory and critical care medicine. 2021;203(2):192-201.
[10]. Suleiman A, Rafaa T, Alrawi A, Dawood M. The impact of ACE2 genetic polymorphisms (rs2106809 and rs2074192) on gender susceptibility to COVID-19 infection and recovery: A systematic review. Baghdad Journal of Biochemistry and Applied Biological Sciences. 2021;2(03):167-80.
[11]. Rubino F, Amiel SA, Zimmet P, Alberti G, Bornstein S, Eckel RH et al. New-onset diabetes in Covid-19. New England Journal of Medicine. 2020;383(8):789-90.
[12]. Bloomgarden ZT. Diabetes and COVID-19. Journal of Diabetes. 2020;12(4):347-8.
[13]. Peric S, Stulnig TM. Diabetes and COVID-19. Wiener Klinische Wochenschrift. 2020;132(13):356-61.
[14]. Fadini G, Morieri M, Longato E, Avogaro dA. Prevalence and impact of diabetes among people infected with SARS-CoV-2. Journal of endocrinological investigation. 2020;43(6):867-9.
[15]. Valencia I, Peiró C, Lorenzo Ó, Sánchez-Ferrer CF, Eckel J, Romacho T. DPP4 and ACE2 in diabetes and COVID-19: therapeutic targets for cardiovascular complications? Frontiers in pharmacology. 2020:1161.
[16]. Powers AC, Aronoff DM, Eckel RH. COVID-19 vaccine prioritisation for type 1 and type 2 diabetes. The Lancet Diabetes & Endocrinology. 2021;9(3):140-1.
[17]. Kohio HP, Adamson AL. Glycolytic control of vacuolar-type ATPase activity: a mechanism to regulate influenza viral infection. Virology. 2013;444(1-2):301-9.
[18]. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes/metabolism research and reviews. 2020;36(7):e3319.
[19]. Montefusco L, Nasr MB, D'Addio F, Loretelli C, Rossi A, Pastore I et al. Acute and long-term disruption of glycometabolic control after SARS-CoV-2 infection. Nature Metabolism. 2021:1-12.
[20]. Qadir MMF, Bhondeley M, Beatty W, Gaupp DD, Doyle-Meyers LA, Fischer T et al. SARS-CoV-2 infection of the pancreas promotes thrombofibrosis and is associated with new-onset diabetes. JCI insight. 2021;6(16).
[21]. Liu F, Long X, Zhang B, Zhang W, Chen X, Zhang Z. ACE2 expression in pancreas may cause pancreatic damage after SARS-CoV-2 infection. Clinical Gastroenterology and Hepatology. 2020;18(9):2128.
[22]. Masamune A, Watanabe T, Kikuta K, Shimosegawa T. Roles of pancreatic stellate cells in pancreatic inflammation and fibrosis. Clinical Gastroenterology and Hepatology. 2009;7(11):S48-S54.