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ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2022;11(1):85-9

Evaluation of the relationship between COVID-19 and hyperglycemia

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Received 15 September 2021; Accepted 20 October 2021
Available online 30.12.2021 with doi: 10.5455/medscience.2021.09.293

Abstract

The coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and enters cells via the angiotensin-converting enzyme. This enzyme is found in many organs, including the pancreas. Thus, the virus enters the pancreatic islets via this enzyme and causes acute hyperglycemia by triggering acute beta-cell dysfunction. Hyperglycemia is an independent risk factor that increases the mortality and morbidity of COVID-19. Therefore, we aimed to evaluate the presence of elevated glucose levels and/or DM in COVID-19 patients and their relationship with clinical findings, biochemical and inflammatory markers, and prognosis of COVID-19. The study included 300 patients. Advanced age (OR: 1.0, 95% CI: 1.0-1.1, p: 0.03) and mutant strain (OR:0.1, 95% CI: 0.1-0.3, p: <0.01) was found to be significant in multivariable logistic regression analysis. Hyperglycemia was observed when CT (p=0.04) involvement increased. COVID-19 infection affects several systems, including the mechanism of blood sugar regulation. The frequencies of intensive care treatment, elevated CRP, increased sedimentation, elevated D-dimer, and mutant strains, 2 of which were Brazilian and 66 British mutations, were significantly higher in hyperglycemic patients without DM. The presence of hyperglycemia at the time of admission has prognostic significance, and the clinician should be more careful in patients with hyperglycemia at the time of admission. Future studies with long-term follow-up of COVID-19 patients may elucidate the causality between COVID-19 and hyperglycemia.

Keywords: COVID-19, hyperglycemia, diabetes mellitus

Introduction

The new coronavirus disease called Coronavirus Disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that first emerged in China at the end of 2019, was considered as a pandemic by the World Health Organization (WHO) in March 2020 [1]. Another important epidemic worldwide is Diabetes Mellitus (DM), which affected 9.3% of the world's population aged 20-79 years in 2019 [2]. Furthermore, DM is demonstrated as the second most common disease accompanying COVID-19 [3]. The SARS-CoV-2 enters cells via the angiotensin-converting enzyme. This enzyme is also found in a wide range of organs such as the lungs, pancreas, kidneys, vascular system, and intestinal endothelium [4]. The virus may also enter the pancreatic islets via this enzyme and cause acute hyperglycemia by triggering acute beta cell dysfunction [5]. Studies have shown that comorbid diseases such as hypertension, DM, cardiovascular disease, acute renal failure increase both the severity and mortality of COVID-19 [3]. It has been shown that elevated lactate dehydrogenase (LDH), CRP, ferritin, D-dimer, low lymphocyte counts, and diffuse computer tomography (CT) findings are associated with poor prognosis of the disease [6].

Therefore, we aimed to evaluate the presence of elevated glucose levels and/or DM in COVID-19 patients and their relationship with clinical findings, biochemical and inflammatory markers, and prognosis of COVID-19. Therefore, we investigated the presence of elevated glucose and/or DM in COVID-19 patients and evaluated clinical findings, biochemical and inflammatory markers. We aimed to evaluate the relationship between hyperglycemia and DM and clinical and laboratory findings and whether there is a prognostic significance.

Materials and Methods

All patients who were hospitalized in Mersin City Training and Research Hospital due to COVID-19 infection between January 01, 2021, and April 01, 2021, had pneumonia on thoracic CT, and were older than 18 years were included and evaluated retrospectively. The results of tests performed within the first 24 hours of hospitalization were included in the study.

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Glucose, hemogram (Hemoglobin [Hb], white blood cell [WBC], lymphocyte, neutrophil), and biochemical parameters (creatinine, aspartate transaminase [AST], alanine aminotransferase [ALT], lactate dehydrogenase [LDH]), inflammatory markers (C-reactive protein) [CRP], procalcitonin, ferritin), the findings of computed tomography scan of thorax (thoracic CT) (GE Healthcare Optima CT660, Chicago, IL, USA) were examined retrospectively. The presence of SARS-CoV-2 was tested using reverse transcription-polymerase chain reaction (RT-PCR) (Bio-Speedy COVID-19 RT-qPCR kit BS-SY-WCOR-305-1000; version 2003261000SK-MK kit) from nasopharyngeal swab and/or deep throat saliva, and patients who tested positive were included. Demographic data, symptoms, comorbid diseases, diabetes mellitus, need for intensive care, treatments were obtained retrospectively from the hospital electronic database.

The severity of COVID-19 disease was defined according to the "Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (7th edition)" guideline [7]. The disease was accepted as mild in case of a mild clinical condition, but normal imaging findings; as moderate in case of fever and respiratory symptoms with imaging findings; and severe in case of a respiratory rate ≥30/min, SpO2 ≤ 93% at rest, and >50% increase in imaging findings within 48 hours (one or more of these). A blood glucose level of 140 mg/dL and above was considered as hyperglycemia, and a blood glucose level below 140 mg/dL was considered as normoglycemia. Patients who have been previously diagnosed with DM by a physician and/or used antidiabetic drugs or insulin were considered DM patients [8].

Data were calculated using the statistical program SPSS 21.0 (IBM Corp., Armonk, NY, USA). The compliance of the variables to the normal distribution was examined using the Kolmogorov-Smirnov test. Mean ± standard deviation (SD) or median (minimum-maximum) was used to define numerical variables, and categorical variables were defined as numbers and percentages. The t-test and Mann-Whitney U test were used to compare numerical variables between the two groups, and the Chi-square or Fisher exact chi-square tests were used for categorical variables. Multivariable logistic regression was used to assess the relationship between hyperglycemic patients and other independent variables. This study was approved by Mersin University Non-invasive Clinical Research Ethics Committee (Decision Date: 23.06.2021, Decision number: 464) and has been prepared in accordance with the principles of the Declaration of Helsinki.

Results

The study included 300 patients. There were 117 (39%) female and 183 (61%) male patients, with a mean age of 53.8±14.4 years. Hypertension was the most common comorbid disease, observed in 106 (35.3%) patients while DM was detected in 28 (8%) patients. In total, 276 (92%) patients had respiratory distress, and the least frequent symptom was the loss of taste and smell, reported by only five (1.7%) patients. The severity of COVID-19 was moderate in 209 (69.7%) patients were moderate. A moderate CT involvement was detected in 261 (87.0%) patients. The mean hospital stay was 10.6±6.9 days. Demographic and laboratory data of the patients are given in Table 1.

Table 1. Demographic and laboratory data of the patients (N=300)

Features	n(%)
Gender	
Female	117(39)
Male	183(61)
Age, mean±SD	53.8±14.4
Comorbidity	
Cardiovascular disease	49(16.3)
Diabetes Mellitus	24(8)
Hypertension	106(35.3)
Respiratory diseases	42(14)
Symptoms	
Fever	135(45)
Sore throat	79(26.3)
Back pain	187(62.3)
Dispne	276(92)
Taste-smell loss	5(1.7)
Oxygen requirement	79(26.3)
CT findings	
Modarete	261(87.0)
Severe	39(13.0)
Clinical findings	
Modarete	209(69.7)
Severe	91(30.3)
Plasmapheresis	3(1)
Cytokine filter	1(0.3)
Intensive care treatment	73(24.3)
İntubated	21(7)
Death	22(7.3)
Days of stay in Hospital	10.6±6.9
Mutant strain *	68(22.7)
WBC, mean±SD	7362±5441
Neutrophil, mean±SD	4936±2746
Lymphocyte, mean±SD	1401±710
HB g/dl, mean±SD	13.6±1.9
Glucose mg/dl, mean±SD	158±81
Creatinine mg/dl, mean±SD	0.99±0.6
AST U/L, mean±SD	42±35
ALT U/L, mean±SD	41±34
LDH U/L, mean±SD	314±111
Sedimentation mm/h, mean±SD	26±18
CRP mg/dl, mean±SD	5.9±5.5
Procalcitonin ng/ml, mean±SD	0.12±0.83
Ferritin ng/ml median (min-max)	228.6 (5-3229)
D-dimer mg/L median (min-max)	0.53 (0.15-21.9)

Data mean ± SD, median (min-max), number (%) as appropriate. Significant P values are indicated in bold.DM: Diabetes Mellitus, HB: Hemoglobin, WBC: White blood cell, AST: Aspartate transaminase, ALT: Alanine aminotransferase, LDH: lactate dehydrogenase, CRP: C-reactive protein
*2 patients with Brazilian mutant strain, others British mutant strain

The comparison between hyperglycemic and normoglycemic/ hyperglycemic without DM and normoglycemic / DM and normoglycemic patients are shown in Table 2. Higher mean age (p<0.01), higher frequencies of intensive care treatment (p=0.04), mutant strain (p<0.01), higher levels of CRP (p=0.05), sedimentation (p=0.03), and D-dimer (p=0.007) were observed in hyperglycemic patients without DM. The frequency of severe CT involvement was higher (p=0.04). Blood glucose was 128 ± 78.6 in patients with moderate CT involvement and 150±9 in patients with severe CT involvement. And hyperglycemia was observed when CT involvement increased. In DM patients, increased oxygen requirement (p=0.001) was statistically higher.

Advanced age (OR:1.0,95%CI:1.0-1.1,p:0.03) and mutant strain (OR:0.1,95%CI: 0.1-0.3,p:<0.01) was found to be significant in multivariable logistic regression analysis. The age and gender adjusted univariable and multivariable logistic regression analysis between hyperglycemic patients without DM and normoglycemic patients is given in Table 3.

Table 2. The comparison between hyperglycemic and normoglycemic/ hyperglycemic without DM and normoglycemic / DM and normoglycemic patients.

	Hyperglycemic patients(include DM)			**Hyperglycemic patients without DM**			**DM**		
	Hyperglycemia (N:125)	**Normoglycemia (N:175)**	**P**	**Hyperglycemia (N:114)**	**Normoglycemia (N:162)**	**P**	**DM (N:24)**	**Normoglycemia (N:276)**	**P**
Features	**n (%)**	**n (%)**		**n(%)**	**n(%)**		**n(%)**	**n(%)**	
Male	77(61.6)	106(60.6)	0.9	68(59.6)	97(59.9)	1	18(75.0)	165(59.8)	0.2
Age	57.6±12.4	51.1±15.1	<0.01	57.7±12.6	51.6±15.0	<0.01	50.3±14.6	54.1±14.4	0.2
CT findings									
Modarete	102(81.6)	159(90.9)	0.02	94(82.5)	148(91.4)	0.04	19(19.2)	242(87.7)	0.2
Severe	23(18.4)	16(9.1)		20(17.5)	14(8.6)		5(20.8)	34(12.3)	
Clinical findings									
Modarete	79(63.2)	130(74.3)	0.04	72(63.2)	119(73.5)	0.08	18(75.0)	191(69.2)	0.6
Severe	46(37.9)	45(25.7)		42(36.8)	43(26.5)		6(25.0)	85(30.8)	
Plasmapheresis	1(1.2)	2(1.7)	1	1(1.4)	2(1.9)	0.8	0(0)	3(1.7)	0.5
Cytokine Filters	1(1.2)	0(0)	0.3	1(1.4)	0(0)	0.2	0(0)	1(0.6)	0.7
Intensive care trement	41(30.4)	32(18.3)	0.04	36(31.6)	31(19.1)	0.02	6(25.0)	67(24.3)	1
Intubated	12(9.6)	9(5.1)	0.1	10(8.8)	9(5.6)	0.3	2(8.3)	19(6.9)	0.8
Oxygen requirment	118(94.4)	158(90.3)	0.2	109(95.6)	150(92.6)	0.4	17(70.8)	259(93.8)	0.01
Days of hospital stays	11.3±7.0	10.1±6.9	0.2	11.3±6.7	10.1±7.1	0.2	11.1±7.3	10.6±6.9	0.7
Death	12(9.6)	10(5.7)	0.2	10(8.8)	10(6.2)	0.5	2(8.3)	20(7.2)	0.8
Mutant strain *	55(44.0)	13(7.4)	<0.01	52(45.6)	11(6.8)	<0.01	5(20.8)	63(22.8)	1
WBC >11000	40(32.0)	55(31.4)	0.9	78(68.4)	113(69.8)	0.9	10(41.7)	85(30.8)	
Neutrophil >8000	21(16.8)	15(8.6)	0.03	96(84.2)	148(91.4)	0.09	4(11.1)	32(11.6)	0.5
Lymphocyte <600	15(9.1)	7(4.0)	0.008	101(90.2)	153(95.6)	0.09	4(11.1)	18(6.6)	0.07
AST>40 U/L	41(32.8)	65(37.1)	0.4	75(65.8)	104(64.2)	0.8	9(37.5)	97(35.1)	0.8
ALT >40 U/L	43(34.4)	56(32.0)	0.7	76(66.7)	112(69.1)		11(45.8)	88(31.9)	0.2
LDH >225 U/L	108(86.4)	134(77.5)	0.05	16(14.0)	36(22.5)	0.09	20(83.3)	222(81.0)	0.8
Sedimentation>20m/h	56(51.3)	56(48.7)	0.03	28(36.4)	54(52.9)	0.03	15(62.5)	97(54.2)	0.5
CRP>0.8 mg/dl	114(91.2)	147(84.0)	0.06	10(8.8)	28(17.3)	0.05	23(95.8)	238(86.2)	0.2
Procalcitonin>0.5ng/ml	7(5.6)	4(2.3)	0.2	107(93.9)	158(97.5)	0.1	0(0)	11(4.0)	0.3
Ferritin >322 ng/ml	57(46.7)	61(37.2)	0.1	61(55.0)	97(64.2)	0.2	14(53.8)	104(39.7)	0.09
D-dimer>0.55 mg/L	69(55.2)	68(38.9)	0.05	51(44.7)	100(61.7)	0.007	12(50.0)	125(45.3)	0.7

Presented as mean ± SD, median (min-max), ornumber (%).Significant P values are indicated in bold. DM: Diabetes Mellitus, HB: Hemoglobin, WBC: White blood cell, AST: Aspartate transaminase, ALT: Alanine aminotransferase, LDH: lactate dehydrogenase, CRP: C-reactive protein
*2 patients with Brazilian mutant strain, others British mutant strain

Table 3. The age- and gender-adjusted univariable and multivariable logistic regression analysis between hyperglycemic patients without DM and normoglycemic patients.

Features	Univariable		Multivariable	
	OR (95% CI)	P-value	OR (95% CI)	P-value
Age	1.0(1.0-1.1)	<0.01	1.0(1.0-1.1)	0.03
Gender	0.9(0.6-1.6)	0.9	0.6(0.2-1.3)	0.2
Clinical findings	1.4(0.8-2.4)	0.2	0.6(0.2-1.8)	0.4
CT findings	2.5(1.2-5.2)	0.01	2.9(0.7-11.5)	0.1
Intensive care treatment	0.6(0.3-1.1)	0.08	0.7(0.3-1.8)	0.5
Mutant strain *	0.1(0.05-0.2)	<0.01	0.1(0.1-0.3)	<0.01
Neutrophil >8000	2.0(0.9-4.3)	0.08	2.7(0.8-9.1)	0.1
Lymphocyte <600	2.0(0.7-5.5)	0.2	1.6(0.4-6.2)	0.5
LDH >225 U/L	1.8(0.9-3.5)	0.08	1.0(0.4-2.7)	0.9
Sedimentation >20 mm/h	2.0(1.1-3.7)	0.03	1.8(0.8-4.0)	0.2
CRP>0.8 mg/dl	1.9(0.8-1.1)	0.1	0.7(0.2-2.4)	0.6
D-dimer>0.55 mg/L	1.6(1.0-2.7)	0.07	1.4(0.6-3.1)	0.4

Significant P values are indicated in bold. CT: Computed tomography, LDH: Lactate dehydrogenase. *2 patients with Brazilian mutant strain, others British mutant strain

Discussion

Our study included 300 COVID-19 patients who received inpatient treatment with moderate/severe CT findings and moderate/severe clinical manifestations. Advanced age (and mutant strain was found to be significant and hyperglycemia was observed when CT (p=0.04) involvement increased. Hospital stays with hyperglycemia without DM patients (11.3±6.7) were longer than normoglycemic patients.

The most common comorbid disease was hypertension in 106 (35.3%) of the patients, while DM was detected in 28 (8%) patients. The prevalence of DM in COVID-19 patients is 8-11% [9-12] in the literature, which is consistent with the prevalence of DM in our study.

SARS-CoV-2 enters cells via the angiotensin-converting enzyme. This enzyme is also found in many organs such as the lungs, pancreas, kidneys, vascular system [4,5]. Hyperglycemia is an independent risk factor that increases the mortality and morbidity of COVID-19 infection. In the case of hyperglycemia, glycosylated ACE2 and glycosylated viral spike protein increase. The binding capacity of the virus and the immune response increase depending on glycosylation [13]. Consequently, hyperglycemia increases both the prevalence and the severity and mortality rates of the disease [14].

In the study performed by Kristan et al. on 829 patients, advanced age was considered as a risk factor in patients with DM [15]. Similarly, advanced age (OR:1.0, 95% CI:1.0-1.1, p:0.03) was found as a risk factor in patients with hyperglycemia in our study.

It has been shown that elevated lactate dehydrogenase (LDH), CRP, ferritin, D-dimer, low lymphocyte counts, and diffuse computer tomography (CT) findings are associated with poor prognosis of the disease [6]. In our study, elevated CRP (p=0.05), increased sedimentation (p=0.03), and elevated D-dimer (p=0.007) were statistically significant in hyperglycemic patients without DM. In addition, hyperglycemia was statistically significantly detected in patients with severe CT findings (OR: 2.5, 95% CI: 1.2-5.2, p: 0.01).

In Turkey, a nationwide retrospective cohort of non-diabetic patients showed that hospital stays longer than eight days were significantly higher [16]. We found that hospital stays with hyperglycemia without DM patients (11.3±6.7) were longer than normoglycemic patients. Zhang et al. showed that hyperglycemia without DM is an increased need for mechanical ventilation, to need for ICU hospitalization [17]. And Saand et al. found that mechanical ventilation rates were significantly higher hıyperglycemia with and/or DM [18]. In our study, ıntensive care treatment (p=0.02) was statistically significant in hyperglycemia without DM and, the oxygen requirement (p=0.01) was higher in patients with pre-existing diabetes mellitus. The literature show that hyperglycemia with and/or DM has been described as a risk factor for worse prognosis in patients with COVID-19 and the findings in our study may be guiding that in patients infected with COVID-19, clinicians should pay attention to hyperglycemia not only in the presence of DM, but also independently of DM.

Of the patients, 68 (22.7%) had mutant strains, 2 of which were Brazilian and 66 British mutations, and having the latter mutant strain (OR:0.1, 95% CI: 0.1-0.3, p: <0.01) was determined as a risk factor. To the best of our knowledge, there are no studies examining the relationship between different strains and hyperglycemia, and it can be concluded that new mutations constitute a risk factor for hyperglycemia.

The strength of the study is based on the fact that it examines the clinical, laboratory, and imaging findings in Turkish patients

with COVID-19 according to hyperglycemia and/or DM and demonstrates the relationship between the new mutant variant and hyperglycemia. The lack of a healthy control group, data on the interventions for blood sugar regulation, long-term follow-up, the retrospective and observational nature of the study are the limitations. Due to the destruction of islet cells in the pancreas with the severe acute respiratory syndrome (SARS), hyperglycemia has been detected in the patient control performed three years later. Accordingly, long-term effects should be followed up, as beta-cell damage occurs similarly in COVID-19 infection [19].

Conclusion

COVID-19 infection affects several systems, including the mechanism of blood sugar regulation. The frequencies of intensive care treatment, elevated CRP, increased sedimentation, elevated D-dimer, and mutant strains, 2 of which were Brazilian and 66 British mutations, were significantly higher in hyperglycemic patients without DM. The presence of hyperglycemia at the time of admission has prognostic significance, and the clinician should be more careful in patients with hyperglycemia at the time of admission. Future studies with long-term follow-up of COVID-19 patients may elucidate the causality between COVID-19 and hyperglycemia.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
Non-invasive clinical ethics committee approval was obtained from Mersin University and has been prepared in accordance with the Declaration of Helsinki principles

References

1. Lui DTW, Lee CH, Chow WS, et al. A territory-wide study on the impact of COVID-19 on diabetes-related acute care. J Diabetes Investig. 2020;11:1303-6.
2. Saeedi P, Petersohn I, Salpea P, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019;157:107843.
3. Zhu N, Zhang D, Wang W, et al. ChinaNovel Coronavirus Investigating and Research Team A novel coronavirus from patients withpneumonia in China, 2019. N Engl J Med. 2020;382:727–33.
4. Li H, Liu SM, Yu XH, et al. Coronavirus disease 2019 (CO VID-19): current statusand future perspectives. Int J Antimicrob Agents. 2020;55:105951.
5. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. 2020;e3319.
6. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of coronavirus disease 2019 in china. N Engl J Med. 2020;382:1708-20.
7. Izumi Y, Hidaka Y, Tada H, et al. Simple and practical parameters for differentiation between destruction-induced thyrotoxicosis and Graves' thyrotoxicosis. Clin Endocrinol (Oxf). 2002;57:51-8.
8. Umpierrez GE, Hellman R, Korytkowski MT, el al. Management of hyperglycemia in hospitalized patients in non-critical care setting: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metabol. 2012;97:16–38.
9. Singh AK, Gupta R, Misra A. Comorbidities in COVID-19: outcomes in hypertensive cohort andcontroversies with renin angiotensin system blockers. Diabetes Metabol Syndrome Res Rev. 2020;14:283-7.
10. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int J Infect Dis. 2020 Mar 12 doi: 10.1016/j.ijid.2020.03.017. pii: S1201-9712(20)30136-3.
11. Epidemiology Working Group for Ncip Epidemic Response The epidemiological characteristics ofan outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Chin J Epidemiol. 2020;41:145–51.
12. Preliminary estimates of the prevalence of selected underlying health conditions among patientswith coronavirus disease 2019 — United States, february 12–march 28, 2020.CDC COVID-19response team.
13. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages isletsand causes acute diabetes. Acta Diabetol. 2010;47.
14. Cheng H, Wang Y, Wang G-Q. Organ-protective effect of angiotensin-converting enzyme 2 and itseffect on the prognosis of COVID-19. J Med Virol. 2020;92:726-30.
15. Kristan MM, Kim YK, Nelson T, et al. Predictors of severe COVID-19 disease in patients with diabetes: a multi-center review. Endocr Pract. 2021;27:842-9.
16. Haymana C, Demirci I, Tasci I, et al. Clinical outcomes of non-diabetic COVID-19 patients with different blood glucose levels: a nationwide Turkish study (TurCoGlycemia). Endocrine. 2021;73:261-9.
17. Zhang Y, Li H, Zhang J, et al. The clinical characteristics and outcomes of patients with diabetes and secondary hyperglycaemia with coronavirus disease 2019: A single-centre, retrospective, observational study in Wuhan. Diabetes Obes Metab. 2020;22:1443-54.
18. Saand AR, Flores M, Kewan T, et al. Does inpatient hyperglycemia predict a worse outcome in COVID-19 intensive care unit patients?. J Diabetes. 2021;13:253-60.
19. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages isletsand causes acute diabetes. Acta Diabetol. 2010;47:193–9.