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Well-controlled vs poorly-controlled diabetes in patients with COVID-19: Are there any differences in outcomes and imaging findings?

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ABSTRACT

Aims: We aimed to compare the clinical outcomes and imaging findings between COVID-19 patients with well-controlled diabetes and those with poorly-controlled diabetes.

Methods: In this retrospective single-center study, 117 patients with coexistent COVID-19 and type 2 diabetes mellitus were included. Patients were divided into two groups based on HbA1c values. Clinical data and laboratory parameters were collected from patients’ medical records. Also, the chest computed tomography (CT) score was defined by the summation of individual scores from 5 lung lobes: scores of 0, 1, 2, 3, 4 and 5 were respectively assigned for each lobe if pulmonary involvement was 0%, less than 5%, 5%-25%, 26%-49%, 50%-75%, or more than 75% of each region.

Results: Among all patients with diabetes, 93 (79.5%) patients had poorly-controlled diabetes and 24 (20.5%) had well-controlled diabetes; 66 (56.4%) patients were male and the median age was 66 years (IQR, 55–75 years). The chest CT severity scores were not significantly different between patients with well-controlled diabetes and those with poorly-controlled diabetes (p = 0.33). Also, the mortality and recovery rates were similar between the two groups (p = 0.54 and p = 0.85, respectively).

Conclusion: Based on the results, clinical outcomes and chest CT severity scores are similar between patients with well-controlled and poorly-controlled diabetes among the Iranian population with COVID-19.

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pandemic, was termed the novel coronavirus disease-2019 (COVID-19). The clinical spectrum of COVID-19 varies widely; while the majority of patients present with a mild form of the disease, severe cases may develop acute respiratory distress syndrome (ARDS), multiple organ failure, and even death [2–4].

Currently, the diagnosis of COVID-19 is confirmed by real-time reverse transcriptase polymerase chain reaction (RT-PCR); however, chest computed tomography (CT) imaging has played a major role in the diagnosis and management of suspected or confirmed cases of COVID-19 [5,6]. In addition, various CT scores have been designed to assess the severity of disease [7–9]. Studies reporting the chest CT findings of COVID-19 have indicated that the most common findings are ground-glass opacities (GGO) and consolidation, which mainly have a peripheral distribution [10,11]. Moreover, chest CT severity scores are higher among severe cases of COVID-19 compared with patients with mild disease [8,9,12].

According to the literature, patients with comorbidities such as diabetes, hypertension, and cardiovascular disease, as well as older patients are prone to worse clinical outcomes and higher rates of complications associated with COVID-19 [3,13,14]. Studies from the previous pandemics including the influenza A (H1N1), SARS-CoV, and MERS-CoV pandemics indicated that diabetes and uncontrolled glycemia were significantly associated with disease severity and mortality in infected patients [15–17]. For example, a study evaluating the 2009 pandemic influenza A (H1N1) virus found that the fasting plasma glucose (FPG) level of H1N1 patients on admission was significantly associated with disease severity [18]. To this point, the role of glycemic control in the prognosis of patients with coexistent diabetes and COVID-19 is not clear. In this study, we aimed to compare the clinical outcomes and imaging findings between COVID-19 patients with well-controlled diabetes and those with poorly-controlled diabetes.

2. Methods

2.1. Study design and participants

We conducted a retrospective single-center study on patients who were admitted to a tertiary care hospital in Tehran, Iran with a suspicion of COVID-19 infection. From a total of 1357 patients with COVID-19, admitted between February 2020 and April 2020, 117 (8.6%) patients had type 2 diabetes mellitus (DM) and were included in our study. Diabetes mellitus was confirmed by reviewing patients’ medical records. No exclusion criteria were considered for this study. The included patients were classified as patients with well-controlled or poorly-controlled DM according to hemoglobin A1c (HbA1c) levels recommended by the American Diabetes Association [19]. Patients with an HbA1c level of more than 7% were regarded as patients with poorly-controlled DM, while those with an HbA1c level of equal to or less than 7% were considered as patients with well-controlled DM.

Due to the unavailability of RT-PCR kits for detection of SARS-CoV-2 early in the outbreak in Iran, patients who had clinical features and chest CT findings highly suggestive of COVID-19 were considered as positive cases and thus, were included in this study. This study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences.

2.2. Demographics and laboratory tests

Baseline demographics of patients were retrieved by collecting data from patients’ electronic medical records. In this study, we assessed the underlying comorbidities (hypertension and cardiovascular disease), duration of diabetes, smoking history and medications [insulin, oral hypoglycemic agents (OHAs), angiotensin-converting enzyme inhibitor/angiotensin II receptor blockers (ACEI/ARBs), statin and diuretics] of all participants. Individuals who had ceased smoking more than 10 years earlier were considered as non-smokers.

Laboratory tests included the total count of leukocytes and lymphocytes, HbA1c, lactate dehydrogenase (LDH), C-reactive protein (CRP), magnesium (Mg), phosphorus (P), calcium (Ca), cardiac troponin I, procalcitonin (PCT), D-dimer, 25-OH-VitD, and zinc. In addition, RT-PCR assay was performed on nasopharyngeal specimens for SARS-CoV-2 detection in all patients with Taqman® Premix TAKARA (TaKaRa, Dalian, China) considering the protocols provided by the manufacturer.

2.3. Chest CT interpretation

All patients underwent chest CT examinations after admission and all CT scans were reported by the same radiologist (with years of experience in CT imaging) to reduce potential bias. The chest CT severity score was defined by the summation of individual scores from 5 lung lobes: scores of 0, 1, 2, 3, 4 and 5 were respectively assigned for each lobe if pulmonary involvement was 0%, less than 5%, 5%-25%, 26%-49%, 50%-75%, or more than 75% of each region. The range of total severity score was from 0 (no involvement) to 25 (maximum involvement).

The predominant patterns on chest CT imaging were classified into five groups: GGO, consolidation, GGO/consolidation (mixed), reverse halo sign and crazy-paving. Other secondary CT findings such as cavity, nodule, pleural effusion, pericardial effusion and lymphadenopathy (LAP) >10 mm were also recorded. Distribution of lung lesions was grouped into three categories: peripheral, peribronchovascular and perihilar. Also, lung opacifications fell into three different categories in terms of morphology: round, linear, or non-specific opacities.

2.4. Statistical analysis

Non-normally distributed continuous data were expressed as median [interquartile range (IQR)] and categorical data were presented as number (percentage). Normal distribution was evaluated by using the Shapiro-Wilk test. Chi-square test was used for comparison of proportions between groups. The differences of parametric and non-parametric continuous data were compared between groups by using the
The imaging findings of patients on chest CT are presented in Table 2. The median total CT severity score was 11 and 10.5 among patients with well-controlled and poorly-controlled DM, respectively (p = 0.33). The highest CT scores were observed in the right lower lobes of patients in both groups. The most common chest CT pattern was GGO (51.3%) followed by consolidation (35%). In addition, 85.5% of the cases had lesions with a peripheral distribution on CT imaging; whereas no perihilar distribution was detected in any patient. In terms of morphology, linear opacities were more frequently observed in patients with poorly-controlled DM; however, this finding had borderline significance (p = 0.08). Among 117 patients with COVID-19 and diabetes, 10 (8.5%) and 43 (36.8%) patients had pleural effusion and hyperinflation on CT imaging, respectively.

### Discussion

In this study, we investigated the clinical outcomes, laboratory parameters, and imaging findings of patients with coexistent diabetes and COVID-19 who were admitted to our hospital between February 2020 and April 2020. Previous studies have reported that comorbidities such as diabetes are associated with an increased risk of death among patients with COVID-19 [3,13,14]. In addition, some have argued that glycemic control may be of great value in the prognosis of patients with coexistent diabetes and COVID-19 [20–22]. The mortality rate of hospitalized patients with coexistent COVID-19 and diabetes was about 22% in this study. Likewise, in a study in the United States, the mortality rate among patients with diabetes and/or uncontrolled hyperglycemia was approximately 29% [23]. These mortality rates are higher than those observed among the general population with COVID-19 [24].

Several hypotheses exist for the role of hyperglycemia in the progression of viral respiratory infections. Elevated blood glucose levels may negatively impact pulmonary function, as well as suppressing the immune system and increasing the production of inflammatory cytokines [25–28]. In addition, angiotensin-converting enzyme 2 (ACE2), one of the main receptors for SARS-CoV-2, is expressed within the pancreas, suggesting that this novel coronavirus can directly damage pancreatic islets [29]. Nevertheless, the impact of hyperglycemia on COVID-19 progression requires further investigation.

Recently, Zhu et al. investigated the association of blood glucose control with clinical outcomes in a large-scale study on 7337 patients with confirmed COVID-19, 952 of who had diabetes [30]. They found that 53.6% of patients with diabetes were male, which is similar to the results of our study (56.4%). Also, they reported a prevalence of 13% for diabetes among the total population of patients with COVID-19, whereas our study found a slightly lower prevalence of 8.6%. In Iran, diabetes has an estimated prevalence of 11.4% among 25–70-year-olds [31]. In another study in Italy, the prevalence of diabetes among patients with COVID-19 was 8.9% [32]. A recent meta-analysis also reported a pooled prevalence of 9% for diabetes among patients with COVID-19 [33]. In the study by Zhu et al., patients with diabetes had a relatively lower median age.
compared with our study (62 versus 66 years, respectively). This could be due to the exclusion of patients older than 75 years in the mentioned study. In line with our study, a higher percentage of patients with well-controlled DM were female, while in patients with poorly-controlled DM male patients constituted a higher percentage. Besides, in parallel with our study, they showed that findings on chest CT imaging were similar between the two groups. However, chest CT imaging evaluations were only limited to bilateral/unilateral lesions in that study.

About 18% of the patients with diabetes developed ARDS in our study; similarly, Zhu et al. reported that ARDS occurred in 17% of patients with diabetes. A major difference between these two studies, however, remains in the definition of well-controlled and poorly-controlled DM. Zhu and colleagues divided patients with diabetes into two groups based on the glycemic variability range; while, in our study, patients with diabetes were classified by long-term glyceric control (HbA1c values). This varying definition might explain the differences in the outcomes found between the study by Zhu et al. and this study. Zhu et al. indicated that patients with well-controlled blood glucose had a markedly lower in-hospital death rate compared with those with poorly-controlled blood glucose. However, our study failed to demonstrate a significant difference in clinical outcomes (recovery and death) between the two groups. Another possible reason for the paradoxical findings between the two studies might be the ethnical and geographical variations between the Chinese and the Iranian population. Our findings

| Table 1 – Demographics and clinical characteristics of patients. |
|---------------------|-------------------|-------------------|------------------|------------------|
| Variables           | Total (n = 117)   | Well-controlled (n = 24) | Poorly-controlled (n = 93) | P-value |
| Age, yrs            | 66 (55–75)       | 75.3 (67–86)       | 62.2 (54.5–72.5)       | <0.001  |
| Sex                 |                   |                   |                  |
| Male                | 66 (56.4)         | 9 (37.5)           | 57 (61.3)          | 0.04    |
| Female              | 51 (43.6)         | 15 (62.5)          | 36 (38.7)          | –       |
| Comorbidities       |                   |                   |                  |
| Hypertension        | 62 (53.0)         | 13 (54.2)          | 49 (52.7)          | 0.89    |
| Cardiovascular disease | 39 (33.3)      | 11 (45.8)          | 28 (30.1)          | 0.14    |
| Smoking history     |                   |                   |                  |
| Smoker              | 7 (6.0)           | 1 (4.2)            | 6 (6.5)            | 1.0     |
| Non-smoker          | 110 (94.0)        | 23 (95.8)          | 87 (93.5)          | –       |
| Duration of diabetes, yrs | 8 (5.5–15) | 10 (4.3–15) | 8 (6–15) | 0.77 |
| PCR assay           |                   |                   |                  |
| Positive            | 72/91 (79.1)      | 14/20 (70.0)       | 58/71 (81.7)       | 0.35    |
| Clinical Outcome    |                   |                   |                  |
| Recovery            | 91 (77.8)         | 19 (79.2)          | 72 (77.4)          | 0.54    |
| Death               | 26 (22.2)         | 5 (20.8)           | 21 (22.6)          | 0.85    |
| ARDS                | 21 (17.9)         | 3 (12.5)           | 18 (19.4)          | 0.56    |
| Medications         |                   |                   |                  |
| Insulin             | 32 (27.4)         | 4 (16.7)           | 28 (30.1)          | 0.18    |
| OHA                 | 52 (44.4)         | 10 (41.7)          | 42 (45.2)          | 0.75    |
| ACEI/ARB            | 42 (35.9)         | 11 (45.8)          | 31 (33.3)          | 0.25    |
| Diuretics           | 16 (13.7)         | 4 (16.7)           | 12 (12.9)          | 0.73    |
| Statin              | 32 (27.4)         | 6 (25.0)           | 26 (28.0)          | 0.77    |
| Laboratory tests    |                   |                   |                  |
| HbA1c, %            | 8.6 (7.5–11)      | 6.6 (6.5–7.0)      | 9.0 (8.0–11.2)     | <0.001  |
| Leukocyte, × 10^9/μL|                   |                   |                  |
| <4                  | 5 (5.2)           | 1 (5)              | 4 (5.2)            | 1.0     |
| 4–10                | 68 (70.1)         | 16 (80)            | 52 (67.5)          | 0.34    |
| >10                 | 24 (24.7)         | 3 (15)             | 21 (27.3)          | 0.39    |
| Lymphocyte/μL       |                   |                   |                  |
| ≤1500               | 56 (61.5)         | 13 (68.4)          | 43 (59.7)          | 0.43    |
| >1500               | 35 (38.5)         | 6 (31.6)           | 29 (40.3)          | 0.55    |
| Troponin, ng/mL     | 0.02 (0.01–0.07)  | 0.04 (0.02–0.2)    | 0.02 (0.01–0.05)   | 0.07    |
| Procalcitonin, ng/mL| 0.29 (0.16–1.19)  | 0.27 (0.17–0.53)   | 0.47 (0.15–1.56)   | 0.46    |
| D-dimer, ng/mL      | 243 (18–549)      | 428 (92–1687)      | 112 (18–542)       | 0.53    |
| LDH, U/L            | 478 (379–693)     | 456 (360–507)      | 481 (389–733)      | 0.41    |
| CRP, mg/L           | 49 (21–70)        | 50 (18–74)         | 49 (22–70)         | 0.92    |
| 25-OH-VitD, ng/mL   | 24 (13–39)        | 14 (5–32)          | 27 (16–41)         | 0.04    |
| Zinc, μg/dL         | 60 (47–71)        | 60 (21–60)         | 60 (48–71)         | 1.0     |
| Mg, mEq/L           | 1.9 (1.7–2.1)     | 2.0 (1.7–2.4)      | 1.9 (1.7–2.1)      | 0.19    |
| P, mg/dL            | 3.1 (2.5–4.2)     | 3.6 (2.5–6.0)      | 3.1 (2.4–4.0)      | 0.23    |
| Ca, mg/dL           | 8.6 (8.2–8.9)     | 8.9 (8.4–9.9)      | 8.5 (8.1–8.8)      | 0.04    |

Data are presented as n (%) and median (IQR).

DM, diabetes mellitus; ARDS, acute respiratory distress syndrome; OHA, oral hypoglycemic agent; ACEI/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; HbA1c, hemoglobin A1c; LDH, lactate dehydrogenase; CRP, C-reactive protein; Mg, magnesium; P, phosphorus; Ca, calcium.
are supported by the most recent study on inpatients with COVID-19 and diabetes; in the CORONADO study, HbA1c values were not associated with death or the primary outcome (mechanical ventilation and/or death) in patients with COVID-19 [34].

Although HbA1c serves as a reliable test for measuring blood glucose values over a period of about three months, and HbA1c values greater than 6.4% indicate impaired glycemic control, it is unknown whether HbA1c values or FPG levels have a more dominant role in determining the prognosis of patients with COVID-19. Acute viral respiratory tract infections are associated with diminished insulin sensitivity [35,36]. Therefore, FPG levels may probably increase during hospitalization even in patients with diabetes who have HbA1c values lower than 7%, which could possibly explain the insignificant differences in clinical outcomes between patients with well-controlled and poorly-controlled DM.

Since the emergence of SARS-CoV-2 in December 2019, chest CT imaging has played a major role in the evaluation of patients with COVID-19. CT severity scores were soon developed to assess disease severity on imaging [10,37]. Studies showed that CT scores were significantly higher in severe cases compared with those in mild cases of COVID-19 [8,9,12]. To date, only one study has investigated the difference in CT scores between the general population and those with diabetes. This study found that chest CT scores were significantly higher among patients with diabetes compared with patients without diabetes [38]. Nevertheless, no study has evaluated CT scores among patients with well-controlled and poorly-controlled DM yet. We observed no significant difference in chest CT scores of patients with well-controlled and poorly-controlled DM. In addition, linear opacities were more frequently observed among patients with poorly-controlled DM than those with well-controlled DM. Linear opacities are also seen more commonly among patients with severe disease [12]. In more than 85% of the cases, pulmonary lesions with a peripheral distribution were observed, which is consistent with findings from previously published studies [39,40].

Currently, there is considerable uncertainty with the use of antihypertensive medications in patients with COVID-19 and underlying comorbidities. While some researchers have recommended the continued use of ACEI/ARBs in patients with COVID-19 [41,42], others have turned against the use of these medications [43–45]. Our results demonstrated that patients with diabetes who were receiving ACEI/ARBs had markedly higher rates of death and lower rates of recovery compared with those who did not take these medications. Although these findings are intriguing, caution should be used in the interpretation of these results and more comprehensive studies on larger populations are needed.

Table 2 – Chest computed tomography findings of patients.

|                         | Total       | Well-controlled | Poorly-controlled | P-value |
|-------------------------|-------------|-----------------|-------------------|---------|
| Total CT severity score | 11 (8–14)   | 10.5 (7.25–12.75) | 11 (8–15)         | 0.33    |
| CT score according to lobe | Right upper lobe | 2 (2.0–3.0)     | 2 (1.25–3.0)     | 2 (2.0–3.0) | 0.52 |
|                         | Right middle lobe | 2 (1.0–2.0)     | 2 (1.0–2.0)     | 2 (1.0–2.0) | 0.61 |
|                         | Right lower lobe | 3 (2.0–3.0)     | 3 (2.0–3.75)     | 3 (2.0–3.0) | 0.69 |
|                         | Left upper lobe | 2 (1.0–3.0)     | 2 (1.0–3.0)     | 2 (1.0–3.0) | 0.11 |
|                         | Left lower lobe | 3 (2.0–3.0)     | 2.5 (2.0–3.0)   | 3 (2.0–3.0) | 0.90 |
| Predominant CT pattern  | GGO         | 60 (51.3)       | 12 (50)          | 48 (51.6) | 0.88 |
|                         | Consolidation| 41 (35)         | 10 (41.7)        | 31 (33.3) | 0.44 |
|                         | GGO/Consolidation (mixed) | 10 (8.5) | 2 (8.3) | 8 (8.6) | 0.96 |
|                         | Crazy-paving | 3 (2.6)         | –                | 3 (3.2) | 1.0  |
|                         | Reverse halo sign | 1 (0.9) | – | 1(1.1) | 1.0  |
| Distribution of lung lesions | Peripheral | 100 (85.5) | 18 (75) | 82 (88.2) | 0.11 |
|                         | Peribronchovascular | 52 (44.4) | 10 (41.7) | 42 (45.2) | 0.75 |
|                         | Perihilar     | –               | –                | – | –  |
| Morphology of lung opacifications | Round | 31 (26.5) | 4 (16.7) | 27 (29) | 0.22 |
|                         | Linear | 25 (21.4) | 2 (8.3) | 23 (24.7) | 0.08 |
|                         | Non-specific | 60 (51.3) | 18 (75) | 42 (45.2) | 0.009 |
| Other specific findings | Nodule | 2 (1.7) | 1 (4.2) | 1 (1.1) | 0.37 |
|                         | Cavity | –               | –                | – | –  |
|                         | Pleural effusion | 10 (8.5) | 4 (16.7) | 6 (6.5) | 0.21 |
|                         | Pericardial effusion | 3 (2.6) | – | 3 (3.2) | 1.0  |
|                         | Lymphadenopathy >10 mm | – | – | – | –  |
|                         | Emphysema | –               | –                | – | –  |
|                         | Fibrosis | 2 (1.7) | – | 2 (2.2) | 1.0  |
|                         | Hyperinflation | 43 (36.8) | 9 (37.5) | 34 (36.6) | 0.93 |

CT, computed tomography; GGO, ground-glass opacity.
4.1. Limitation

This study has several limitations. First, the number of cases in each group was markedly different, which necessitates a careful interpretation of the results. Larger prospective studies among different populations are needed to explore the association between diabetes, either well-controlled or poorly-controlled, and imaging findings and clinical outcomes. Also, as mentioned earlier, we did not evaluate patients’ blood glucose tests during hospitalization and so, our assumption of glycemic control in patients with diabetes was solely based on HbA1c values.

5. Conclusion

This retrospective single-center study showed that patients with well-controlled or poorly-controlled diabetes did not significantly differ in terms of clinical outcomes and chest CT severity scores.

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Declarations of interest

None.

REFERENCES

[1] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with Pneumonia in China, 2019. N Engl J Med 2020;382(8):727–33.
[2] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. novel coronavirus in Wuhan, China. The Lancet 2019;2020:395.
[3] Guan W-J, Ni Z-Y, Hu Y, Liang W-H, Ou C-Q, He J-X, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020;382(18):1708–20.
[4] Peng Q-Y, Wang X-T, Zhang L-N. Chinese Critical Care Ultrasound Study G. Findings of lung ultrasonography of novel corona virus pneumonia during the 2019–2020 epidemic. Intensive Care Med 2020.
[5] Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. COVID-19 in China: a report of 1014 cases. Radiology 2020;200642.
[6] Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. Radiology 2020;200343.
[7] Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19). Radiology 2020;295(3):715–21.
[8] Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, et al. CT image visual quantitative evaluation and classical classification of coronavirus disease (COVID-19). Eur Radiol 2020.
[9] Yang R, Li X, Liu H, Zhen Y, Zhang X, Xiong Q, et al. Chest CT Severity Score: An Imaging Tool for Assessing Severe COVID-19. Radiol: Cardiothoracic Imag 2020;2(2):e200047.
[10] Chung M, Bernheim A. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology 2020;295(1):202–7.
[11] Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, et al. Emerging 2019 Novel Coronavirus (2019-nCoV) Pneumonia. Radiology 2020;295(1):210–7.
[12] Li K, Wu J, Wu F, Guo D, Chen L, Fang Z, et al. The Clinical and Chest CT Features Associated With Severe and Critical COVID-19 Pneumonia. Invest Radiol 2020;55(6):327–31.
[13] Yang X, Yu Y, Xu J, Shu H, Ja X, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475–81.
[14] Zhang H, Dong X, Cao Y, Du Y, Yan Y, Yan Q, et al. Clinical characteristics of 140 patients with infected with SARS-CoV-2 in Wuhan, China. Allergy 2020.
[15] Banik GR, Alqehani AS, Booy R, Rashid H. Risk factors for severity and mortality in patients with MERS-CoV. Analysis of publicly available data from Saudi Arabia. Virol Sin 2016;31(1):81–4.
[16] Schoen K, Horvat N, Guerreiro NFC, de Castro I, de Giassi KS. Spectrum of clinical and radiographic findings in patients with diagnosis of H1N1 and correlation with clinical severity. BMC Infect Dis 2019;19(1):964.
[17] Yang J, Liu Y, Yuan MY, Yuan SY, Fu HJ, Wu BY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabet Med 2006;23(6):623–8.
[18] Wang W, Chen H, Li Q, Qiu B, Wang J, Sun X, et al. Fasting plasma glucose is an independent predictor of severity of H1N1 pneumonia. BMC Infect Dis 2011;11(1):104.
[19] Standards of Medical Care in Diabetes—2020 Abridged for Primary Care Providers. Clin Diab 2020;38(1):10–38.
[20] Zhou J, Tan J. Diabetes patients with COVID-19 need better blood glucose management in Wuhan, China. Metabolism 2020;107:154216–.
[21] Hill MA, Mantzoros C, Sowers JR. Commentary: COVID-19 in patients with diabetes. Metabolism 2020;107 154217.
[22] Wei X, Zhao W, Wang A, Xu Z. Timely glucose monitoring-related potential risk of occupational exposure during the pandemic of COVID-19: A diabetologist’s perspective. Diab Res Clin Pract 2020.
[23] Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, et al. Glycemic Characteristic and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States. J Diab Sci Technol 2020. 1932968202092446.
[24] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet 2020;395(10223):507–13.
[25] Haia CCW, Raskin P. The diabetic lung: Relevance of alveolar microangiopathy for the use of inhaled insulin. Am J Med 2005;118(3):205–11.
[26] Goldman MD. Lung Dysfunction in Diabetes. Diab Care 2003;26(6):1915–8.
[27] Kiselar JC, Wang X, Dubyak GR, El Sanadi C, Ghosh SK, Lundberg K, et al. Modification of β-Defensin-2 by Dicarbonyls Methylglyoxal and Glyoxal Inhibits Antibacterial and Chemotactic Function In Vitro. PLoS ONE 2015;10(8):e0130353.
[28] Knapp S. Diabetes and infection: is there a link?—A mini-review. Gerontology 2013;59(2):99–104.
[29] Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat Microbiol 2020;5(4):562–9.
[30] Zhu L, She ZG, Cheng X, et al. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. Cell Metab 2020;31(6):1068–1077.e3. https://doi.org/10.1016/j.cmet.2020.04.021.
[31] Esteghamati A, Etmed K, Kooppayehzadeh J, Abbasi M, Meyسامی A, Noshad S, et al. Trends in the prevalence of diabetes and impaired fasting glucose in association with...
obesity in Iran: 2005–2011. Diab Res Clin Pract 2014;103 (2):319–27.

[32] Fadini GP, Morieri ML, Longato E, Avogaro A. Prevalence and impact of diabetes among people infected with SARS-CoV-2. J Endocrinol Invest 2020;43(6):867–9.

[33] Wang X, Wang S, Sun L, Qin G. Prevalence of diabetes mellitus in, novel coronavirus: A meta-analysis. Diab Res Clin Pract 2019;2020. 164.

[34] Cariou B, Hadjadj S, Wargny M, Pichelin M, Al-Saleh A, Allix I, et al. Phenotypic characteristics and prognosis of patients with COVID-19 and diabetes: the CORONADO study. Diabetologia 2020.

[35] Kotas Maya E, Medzhitov R. Homeostasis, Inflammation, and Disease Susceptibility. Cell 2015;160(5):816–27.

[36] Šestan M, Marinović S, Kavazović I, Cekinović Đ, Wueest S, Turk Wensveen T, et al. Virus-Induced Interferon-γ Causes Insulin Resistance in Skeletal Muscle and Derails Glycemic Control in Obesity. Immunity 2018;49(1). 164 77.e6.

[37] Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multi-center study in Wenzhou city, Zhejiang, China. J infect 2020;80(4):388–93.

[38] 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. Diab/Metabol Res Rev n/a(n/a):e3519.

[39] Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation Between Chest CT Findings and Clinical Conditions of Coronavirus Disease (COVID-19) Pneumonia: A Multicenter Study. Am J Roentgenol 2020;214(5):1072–7.

[40] Zhou S, Wang Y, Zhu T, Xia L. CT Features of Coronavirus Disease 2019 (COVID-19) Pneumonia in 62 Patients in Wuhan, China. Am J Roentgenol 2020;214(6):1287–94.

[41] Peng YD, Meng K, Guan HQ, Leng L, Zhu RR, Wang BY, et al. Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV. Zhonghua Xin Xue Guan Bing Za Zhi. 2020;48:E004.

[42] Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin-Angiotensin-Aldosterone System Inhibitors in Patients with Covid-19. N Engl J Med. 2020;382 (17):1653–9.

[43] Zheng Y-Y, Ma Y-T, Zhang J-Y, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol 2020;17(5):259–60.

[44] Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med 2020;8(4):e21-e.

[45] Cure E, Cumhur Cure M. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic. Diab Metabol Syndrome: Clin Res Rev 2020;14(4):349–50.