Original Article

Investigation of the Relationship between Diabetes Mellitus or Hypertension and the Chest Computed Tomography Scan and Short-term Clinical Outcome in Coronavirus Disease 2019 Pneumonia

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Abstract

Aims: This study aims to investigate the relationship between diabetes mellitus (DM) or hypertension and the distribution and severity of pulmonary involvement and short-term clinical outcome in patients with coronavirus disease 2019 (COVID-19) pneumonia. **Materials and Methods:** In this case–control study, a group of patients with DM and COVID-19 pneumonia are compared to a group without DM. Demographic information, history of diabetes, hypertension, renal disease, tobacco use, laboratory data, current blood pressure, and chest computed tomography (CT) scan of all patients were extracted. The patients' laboratory tests were performed on the same day that the chest CT scan was performed. The data were analyzed using appropriate statistical tests. **Findings:** The results show that gender, age, smoking, and history of kidney disease were not significantly associated with the history of diabetes and hypertension ($P > 0.05$). Furthermore, the history of diabetes and hypertension had no significant relationship with the distribution and severity of pulmonary involvement and short-term clinical outcome ($P > 0.05$). However, among the laboratory findings, hemoglobin, hematocrit, and erythrocyte sedimentation rate were significantly associated with a history of diabetes and blood urea nitrogen values were associated with a history of hypertension ($P < 0.05$). **Conclusion:** Based on the findings of this study, it can be concluded that the history of diabetes and hypertension has no significant relationship with the distribution and severity of pulmonary involvement and short-term clinical outcome.

Keywords: COVID-19, diabetes mellitus, hypertension, pneumonia, pulmonary involvement, severity, short-term clinical outcome

Introduction

The new variant of the coronavirus, SARS-CoV-2, was first reported in Wuhan, China, in December 2019. The rapid spread of the disease and extensive mortality caused by this virus attracted a lot of attention so the WHO declared it a State of Emergency. The total number of confirmed cases of coronavirus disease 2019 (COVID-19) as of December 2022 is more than 660 million, with more than 6.6 million deaths, giving a 1% mortality rate.[1]

Received: 09-Mar-2022 **Revised:** 26-Dec-2022
Accepted: 27-Dec-2022 **Published:** 19-Apr-2023

Access this article online

Quick Response Code:

Website: http://iahs.kaums.ac.ir

DOI: 10.4103/iahs.iahs_55_22

The standard diagnostic test for this viral infection is reverse transcription–polymerase chain reaction (RT-PCR). However, the high false-negative rate at the first-time sampling, lack of widespread availability, and the rapid increase in the number of people with COVID-19 pneumonia make it inappropriate to rely only on RT-PCR as the diagnostic tool or prerequisite

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How to cite this article: Talari H, Jalilizadeh E, Najafizadeh M, Azadbakht J, Sayyah M, Tabatabaei SM. Investigation of the relationship between diabetes mellitus or hypertension and the chest computed tomography scan and short-term clinical outcome in Coronavirus Disease 2019 pneumonia. Int Arch Health Sci 2022;9:158-63.

test for beginning the treatment.[2] Meanwhile, chest computed tomography (CT) scan can play a key role in rapid diagnosis of patients with COVID-19 pneumonia before preparing the test result of RT-PCR, or assessing the severity of pulmonary involvement, as early detection of the disease and starting treatment timely could be clinically important. Based on multiple studies, chest X-ray has a low sensitivity for the diagnosis of COVID-19 pneumonia, so if diagnostic imaging is intended to be performed, chest CT scan would be the choice.[3,4] Recent studies have suggested that the chest CT scan is more sensitive than RT-PCR for the diagnosis of COVID-19 pneumonia.[5-7]

Since the beginning of COVID-19 pandemic in China, many studies have been published on chest CT scan findings of the disease, all of which have described ground-glass opacities and consolidations as the most common findings, often with involvement of both lungs, preferentially with peripheral and lower zone distribution. Crazy paving, reverse halo, and nodular and reticular opacities are also seen, although less common.[4,8-11] The disease course in some patients with COVID-19 pneumonia leads to acute respiratory failure, and some of them die shortly after the onset of the disease as a result of multiple organ failure.[12]

The virus is transmitted from human to human through entering the cells via the angiotensin-converting enzyme 2 (ACE-2) receptor, which has the function of accelerating the conversion of angiotensin 2 to angiotensin 1–7, as well as plays an anti-inflammatory and antioxidant role.[13-15] The ACE-2 plays a key role in multiple organ failures in patients with COVID-19 pneumonia, such as the cardiovascular system, kidneys, lungs, and brain. In patients with diabetes mellitus (DM), ACE-2 expression is probably due to decreased glycosylation, which may justify the increased severity of pulmonary involvement and acute respiratory failure in patients with COVID-19 pneumonia.[15,16]

DM is one of the leading causes of death worldwide, and its mortality rate is expected to increase in the upcoming decades.[17] Various studies have pointed to the fact that patients with DM are at a higher risk for infectious diseases due to impaired immune regulation. Plasma glucose levels and DM are independent predictors of mortality and morbidity in patients with COVID-19 pneumonia.[18-22]

This study is aimed to evaluate the clinical, laboratory, chest CT scan, and short-term clinical outcome of patients with COVID-19 pneumonia and DM to assess any potential relationship between them, and if it is possible to predict the clinical course of the disease using the chest CT scan and laboratory data.

Materials and Methods

This case–control study was performed in two groups of patients with COVID-19 pneumonia older than 40 years who were referred to Shahid Beheshti Hospital, Iran, Kashan over a 3-month period. Inclusion criteria were as follows: patients with RT-PCR-confirmed COVID-19 pneumonia who underwent a chest CT scan upon coming to the hospital and had complete blood count with differential, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, blood urea nitrogen (BUN), creatinine, erythrocyte sedimentation rate (ESR), C-reactive protein, and fasting blood sugar (FBS) tests. In the case group, the patients had a known DM with a history of receiving insulin or oral diabetes medications and were under treatment by an endocrinologist. The criteria for diagnosis of DM were considered as follows: FBS ≥126 mg/dL (7.0 mmol/L) (fasting is defined as no caloric intake for at least 8 h), or 2-h postprandial plasma glucose ≥200 mg/dL (11.1 mmol/L) during oral glucose tolerance test, or hemoglobin (Hb) $A1_C$ ≥6.5% (48 mmol/mol). The criteria for diagnosis of hypertension were as follows: systolic blood pressure values of 130 mmHg or more and/or diastolic blood pressure of more than 80 mmHg.[23]

The patients in the control group had no history of diabetes, and their FBS or random blood sugar (BS) was normal. The control group was matched to the case group by age and sex. All patients who met the inclusion criteria for 2 months were included in the study consecutively. Finally, 41 patients met the inclusion criteria as the case group, which were matched randomly with a group of 41 patients as the control group.

Demographic data, medical history, and laboratory test results of all patients were extracted from the hospital database. Chest CT scans of the patients were also extracted from the picture archiving and communication system (PACS) of the hospital. In cases with more than one chest CT scan, the first CT scan on admission was considered for interpretation. The duration of diabetes and hypertension from the time of diagnosis was also recorded.

All chest CT scans were performed using the Multi-Detector Scanner (Alexion, TSX-034A, Toshiba, Japan) in the Radiology Department of (Shahid Beheshti hospital, Kashan, Iran). A low-radiation dose protocol was applied for the chest CT scans (tube voltage: 120 kVp, tube current: 50–90 mA with automatic exposure control, and slice thickness: 3 mm). CT scans were performed in deep inspiration, and the patient's arms were placed over his head. No oral or intravenous contrast was used.

Two radiologists independently interpreted the CT scans, using the MARCO PACS system. All images were seen in both mediastinal and lung windows. Lung parenchyma images were interpreted at window width – 1600 HU and window level – 550 HU, and mediastinal images at window width – 400 HU and window level – 40 HU. CT scan results were defined based on Fleischner's standard definitions. Radiologists categorized the CT scan findings into ground-glass opacities, consolidation, and other findings (crazy paving, reverse halo sing, air bronchogram, and reticular opacities). Each of the five pulmonary lobes was visually scored from 0 to 5 based on the percent of involvement, providing a total score ranging from 0 (no involvement) to 25 (maximum involvement). Finally, the results of interpretation by the two radiologists were compared, using a consensus approach.

The short-term clinical outcome (based on a 4-week follow-up) was categorized as follows: no need for intensive care unit (ICU) hospitalization, ICU hospitalization, or death.

The study protocol was approved by the Institutional Review Board (IRB) and Ethics Committee of (Kashan University of Medical Sciences). It is in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. All personal information of the patients remained confidential.

Categorical variables were expressed as numbers and percentages. The percentages were compared using the Chi-square test. One-way ANOVA and regression analysis were applied for continuous variables. All statistical analyzes were performed using SPSS version 22 (SPSS Inc., Chicago, IL, USA) software. $P < 0.05$ was considered statistically significant.

The study protocol was approved with the IRB approval code of IR.KAUMS.MEDNT.REC.1399.224. All information remains confidential.

Results

Among all 82 patients studied, 37 had a history of hypertension. The mean and standard deviation of age in diabetic patients was 64.27 ± 11.76 and in nondiabetic patients was 64.29 ± 11.43 years. The mean and standard deviation of age in patients with and without hypertension was 66.35 ± 11.70 and 62.58 ± 11.22 years, respectively. In terms of patients' gender, 16 (39%) males and 25 (61%) females were present in the diabetic group, whereas there were 18 (43.9%) females and 23 (56.1%) males in the nondiabetic group. There were 21 (56.8%) females and 16 (43.2%) males in the hypertension group. In the nonhypertensive group, 23 (51.1%) males and 22 (48.9%) females were present. Based on the statistical analysis, no significant difference was observed between patients with and without hypertension regarding their gender ($P = 0.626$). Other demographic data and medical history of the patients based on the history of diabetes or hypertension are presented in Table 1. The information presented in this table shows that the variables of sex, age, smoking, and history of renal disease were not significantly associated with a history of diabetes and hypertension ($P > 0.05$).

The relationship between the distribution and severity of pulmonary involvement, laboratory findings, and short-term outcome were also analyzed based on the presence of diabetes or hypertension. The information is shown in Table 2.

The results suggest that a history of diabetes or hypertension has no significant relationship with the distribution and severity of pulmonary involvement and short-term clinical outcome ($P > 0.05$). In the laboratory findings, the level of Hb in the nondiabetic group (13.1 g/dl) was significantly higher than in the diabetic group (13.9 g/dl) ($P = 0.043$). Subsequently, the hematocrit (HCT) level in the nondiabetic group (37.2%) was significantly higher than in the diabetic group (39.6%) ($P = 0.019$). Furthermore, the ESR level in the diabetic group (35 mm/h) was significantly higher than in the nondiabetic group (26 mm/h) ($P = 0.045$). Other laboratory findings did not show a significant difference between diabetic and nondiabetic patients ($P > 0.05$). Blood urea nitrogen (BUN) levels in patients with hypertension (21 mg/dl) were significantly higher than in the nonhypertensive group (16 mg/dl) ($P = 0.017$). Other laboratory data did not show a statistically significant difference between hypertensive and nonhypertensive patients ($P > 0.05$).

Discussion

The present study aimed to investigate the relationship between DM and hypertension and the distribution and severity of pulmonary involvement and short-term clinical outcome in patients with COVID-19 pneumonia. The results of our study showed that a history of DM and hypertension had no significant relationship with the distribution and severity of pulmonary involvement and short-term clinical outcome. Among the laboratory findings, Hb, HCT, and ESR values were significantly associated with a history of diabetes, and higher BUN was significantly associated with a history of hypertension.

We observed that a history of DM was not significantly associated with the distribution and severity of pulmonary involvement and short-term clinical outcome. In a study by Khalili *et al*. which compared the mortality rate of COVID-19 pneumonia between two groups of patients with and without DM, no statistically significant difference was found, a finding that is in line with the results of our research. The study found that aging, macrovascular complications of DM, and underlying comorbidities could increase the mortality in people with DM. Insulin therapy during hospitalization was also found to reduce the harmful effects of high BS and improve the prognosis of patients with COVID-19 and underlying DM.[24] However, in some meta-analyses, a positive relationship between the presence of DM and the severity of COVID-19 pneumonia is identified.[25-29] de Almeida-Pititto *et al*. reported a significant increase in mortality from COVID-19 pneumonia among patients with DM.[30]

Based on the results of our study and its comparison to other studies, it can be said that this difference in results may be due to differences in the sample size, differences in inclusion criteria, and differences in patient classification based on demographic variables. Although the results of meta-analysis studies confirm the results of smaller studies, due to the very diverse inclusion criteria in regional, cross-sectional, and cohort studies, these studies are not able to match all conditions and it is very difficult for these researchers to consider all criteria. However, multiple pathophysiological mechanisms

Table 1: Descriptive characteristics of individuals in terms of demographic data and history of diabetes mellitus and hypertension

Variable	Diabetic			HTN		
	Yes	No	*P*	Yes	No	*P*
Gender						
Male	16 (39.0)	23 (56.1)	0.185	16 (43.2)	23 (51.1)	0.626
Female	25 (61.0)	18 (43.9)		21 (56.8)	22 (48.9)	
Age	64.27±11.76 (45-87)	64.29±11.43 (42-86)	0.992	66.35±11.70 (42-87)	62.58±11.22 (42-86)	0.141
Smoking	2 (4.9)	0	0.494	1 (2.7)	1 (2.2)	1.000
Kidney disease	2 (4.9)	8 (19.5)	0.092	6 (16.2)	4 (8.9)	0.503
Duration of diabetes	9.51±6.94 (1-30)	-	-	-	-	-
Type of diabetes						
Controlled	16 (39.0)					
Uncontrolled	25 (61.0)	-	-	-	-	-
Duration of HTN	-	-	-	9.38±7.69 (1-30)	-	-
Type of HTN						
Pre				10 (27.0)		
Stage I				12 (32.5)		
Stage II	-	-	-	15 (40.5)	-	-

HTN: Hypertension

Table 2: The relationship between diabetes and blood pressure with the distribution and severity of pulmonary involvement, laboratory findings, and short-term outcome

Variable	Diabetic			HTN		
	Yes	No	*P*	Yes	No	*P*
CT scan						
CT severity score	8.78±4.27	8.90±3.75	0.891	8.19±4.00	9.38±3.95	0.181
Laterality (two-side)	40 (97.6)	40 (97.6)	1.000	36 (97.3)	44 (97.8)	1.000
Peripheral	41 (100.0)	41 (100.0)	-	37 (100.0)	45 (100.0)	-
Central	30 (73.2)	30 (73.2)	1.000	28 (75.7)	32 (71.1)	0.831
Right upper lobe	38 (92.7)	38 (92.7)	1.000	35 (94.6)	41 (91.1)	0.860
Right middle lobe	37 (90.2)	34 (82.9)	0.517	32 (86.5)	39 (86.7)	1.000
Right lower lobe	41 (100.0)	39 (95.1)	0.494	37 (100.0)	43 (95.6)	0.563
Left upper lobe	37 (90.2)	38 (92.7)	1.000	33 (89.2)	42 (93.3)	0.786
Left lower lobe	40 (97.6)	40 (97.6)	1.000	36 (97.3)	44 (97.8)	1.000
Ground-glass opacity	41 (100.0)	41 (100.0)	-	37 (100.0)	45 (100.0)	-
Consolidation	36 (87.8)	36 (87.8)	1.000	31 (83.8)	41 (91.1)	0.503
Crazy paving	17 (41.5)	11 (26.8)	0.244	14 (37.8)	14 (31.1)	0.685
Reverse halo	13 (31.7)	5 (12.2)	0.062	9 (24.3)	9 (20.0)	0.839
Air bronchogram	22 (53.7)	20 (48.8)	0.825	19 (51.4)	23 (51.1)	1.000
Laboratory						
White blood cell count	5.5 (4.45-7.15)	5.5 (4.8-7.55)	0.670	5.5 (4.45-6.92)	5.5 (4.7-7.7)	0.720
Hemoglobin	13.1 (11.85-14.15)	13.9 (12.7-15.05)	0.043	13.6 (12.65-14.8)	13.1 (11.85-14.5)	0.354
Hematocrit	37.2 (35.3-40.1)	39.6 (36.85-43.1)	0.019	38.3 (36.75-42.75)	37.7 (34.6-41.1)	0.286
ESR	35 (25-55.5)	26 (12.5-43)	0.045	31 (14-45)	32 (16.5-48)	0.852
CRP	36 (11.5-63)	48 (28.5-62)	0.163	38 (11.5-63)	44 (22-61.5)	0.621
BUN	19 (14.5-25)	17 (12.5-23.5)	0.273	21 (15-26)	16 (11.5-23)	0.017
Cr	1.1 (0.9-1.45)	1.1 (0.9-1.25)	0.600	1.1 (0.9-1.45)	1 (0.9-1.2)	0.149
Outcome						
Admission to ICU	31 (75.6)	31 (75.6)	1.000	28 (75.7)	34 (75.6)	1.000
Death	14 (34.1)	10 (24.4)	0.467	7 (18.9)	17 (37.8)	0.104
Hospital stay length (day)	8 (5-12)	8 (5.5-11.5)	0.955	8 (5-10)	8 (5-12.5)	0.740

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, BUN: Blood urea nitrogen, Cr: Creatinine, HTN: Hypertension, ICU: Intensive care unit, CT: Computed tomography can support the association between DM and the severity of COVID-19. Deficiency of the innate immune system due to chronic hyperglycemia, a preinflammatory condition, with improper and stormy cytokine response can be the underlying pathologic mechanisms.[31,32]

In this study, a history of hypertension was not significantly associated with the distribution and severity of pulmonary involvement and short-term clinical outcome of COVID-19 pneumonia. Many studies have shown an increase in the severity of coronavirus pneumonia in patients with hypertension. However, in some studies, such as Lippi *et al*., no association was found between hypertension and disease severity, which is consistent with the findings of our study.[33] However, in the study of de Almeida-Pititto *et al*., a direct and significant relationship was observed between high blood pressure and the severity of COVID-19 pneumonia.[30] In the case of hypertension, Pranata *et al*., in a meta-analysis, examined the association between hypertension with severity and mortality of COVID-19 in a total of 6560 patients. Researchers in this study found that the diagnosis of hypertension was associated with increased mortality and severity of COVID-19, which is not in line with our findings.[34] However, the association between high blood pressure and the worse consequences of COVID-19 infection and the increased severity of the disease may be due to the greater prevalence of comorbidities and the more advanced age of these individuals. However, in confirmation of this theory in an Italian cross-sectional study, hypertension was not introduced as an independent factor influencing the outcome of COVID-19.[35]

This study had some limitations. Not all patients' laboratory tests were repeated to evaluate the progression or improvement of the disorders. Furthermore, the time spent from the onset of symptoms to performing chest CT was not equal for all patients.

Conclusion

Based on the findings of this study, it can be concluded that the history of diabetes and hypertension has no significant relationship with the distribution and severity of pulmonary involvement and short-term clinical outcome. Studies with larger sample sizes and multicenters are recommended to achieve more accurate results.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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