Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Epidemiology and Global Health 16 (2022) 101107

Contents lists available at ScienceDirect

Clinical Epidemiology and Global Health

journal homepage: www.elsevier.com/locate/cegh

Original article

Chest X-Ray pattern and lung severity score in COVID-19 patients with diabetes mellitus: A cross sectional study

Aswin Gunawan Christanto *, Dian Komala Dewi, Harry Galuh Nugraha, Irma Hassan Hikmat

Faculty of Medicine, Universitas Padjajaran, Bandung, Indonesia

ARTICLE INFO

Keywords:
COVID-19
Diabetes mellitus
X-ray
Chest
BRIXIA score

ABSTRACT

Background: Diabetes mellitus is a chronic hyperglycemic condition that can affect the body's immune response to SARS-CoV-2 This study aimed to determine the relationship between diabetes mellitus and lung severity in COVID-19 patients. Methods: A cross-sectional design was conducted at Hasan Sadikin General Hospital during the January–May 2021 period. Data were based on medical records of patients aged 18 years and over with COVID-19. The chi-square test was performed to assess the relationship between diabetes mellitus and lung severity based on the BRIXIA score. Results: This study included 538 subjects, mostly aged <60 years (71.9%) and female (60.2%). A total of 125 subjects had abnormal blood glucose levels with an average HbA1c of 9.00 ± 1.77% in patients with diabetes mellitus and a median HbA1c of 5.85% (4.5–6.4%) in patients with reactive hyperglycemia. Lung abnormalities were found in 357 subjects (66.4%). The results of the BRIXIA score to assess lung severity found as many as 77 subjects (14.3%) had a score of 11–18 with 14 people with diabetes mellitus, five people with reactive hyperglycemia. In the population aged ≥60 years, as many as 32 people had a score of 11–18 with three people with diabetes mellitus, two with reactive hyperglycemia and 27 with normal blood glucose. A significant relationship was found between diabetes mellitus and lung severity ($p = 0.024$). Conclusion: There is a significant relationship between diabetes mellitus and lung severity in COVID-19 patients aged ≥60 years.

1. Introduction

Coronavirus disease 2019 (COVID-19) is an infection caused by severe respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The COVID-19 infection was declared a pandemic by the World Health Organization (WHO) because of its rapid spread from China to various countries around the world. As of January 13, 2022, there were 315, 345, 967 confirmed cases of COVID-19 worldwide.[2] In Indonesia, there were 4, 268,890 confirmed cases with a death toll of 144,155 cases.[3] Diabetes mellitus along with hypertension, cardiovascular disease, smoking, chronic obstructive pulmonary disease, malignancy and chronic kidney failure were the most common comorbidities in patients hospitalized with COVID-19.[4,5]

Diabetes mellitus is a chronic hyperglycemic condition that can affect the body's immune response to SARS-CoV-2. The condition of acute or reactive hyperglycemia can also affect the body's immune response, regardless of the condition of diabetes mellitus or not.[6] Data in Wuhan, China, found that as many as 51% of patients with COVID-19 came in a state of hyperglycemia.[7] Diabetes mellitus is one of the factors that play a role in the outcome of patients with COVID-19. The presence of diabetes mellitus is associated with higher morbidity and mortality.[8–11] The relationship between diabetes mellitus and lung severity in COVID-19 patients has not been widely studied. A study by Iacobellis in Miami found that high blood glucose conditions at admission could be a predictor of lung severity, regardless of the previous history of diabetes mellitus.[12] Therefore, this study aimed to determine the relationship between diabetes mellitus and lung severity in COVID-19 patients.

2. Materials and methods

The research method used was analytic observational with a cross-sectional design. The research data were taken based on medical records of patients with COVID-19 who were treated at Hasan Sadikin

* Corresponding author. Faculty of Medicine- Hasan Sadikin Hospital , Universitas Padjajaran, Jl Pasteur No.38, Pasteur, Kec. Sukajadi, Kota Bandung, Jawa Barat, 40161, Bandung, Indonesia.,

E-mail addresses: dr_aswin@hotmail.com (A.G. Christanto), dkd.radiologi@gmail.com (D. Komala Dewi), hg.nugraha@gmail.com (H.G. Nugraha), irmahassan180@gmail.com (I.H. Hikmat).

https://doi.org/10.1016/j.cegh.2022.101107
Received 25 April 2022; Received in revised form 21 June 2022; Accepted 26 June 2022
Available online 29 June 2022

General Hospital during the January–May 2021 period. Patients aged 18 years and over who were confirmed to have COVID-19 by polymerase chain reaction (PCR) test were included in the study. All participants had performed conventional chest radiography with antero-posterior (AP) projection using Philips Medical System Type SRO 33100 and reviewed by experienced thorax consultant radiologists. Chest radiography features findings was noted to the medical records. Patients were excluded if they had lung disease other than COVID-19 and incomplete medical record data.

Descriptive data in the form of age, gender, diabetes mellitus status and lung conditions are presented in tabular form. Pulmonary conditions consist of lung severity based on the BRIXIA score, the location of the infected lung, the predominance of the abnormal lung area and the presence of pleural effusion. The diagnosis of diabetes mellitus is made if the patient has HbA1c with a value of >6.5% or has previously been diagnosed with diabetes mellitus. If high blood sugar levels are found without a previous history of diabetes mellitus, it is categorized as reactive hyperglycemia. The BRIXIA score is divided into 0–10 and 11–18 based on the study of Au-Yong et al., where a score of 11 and above is associated with decreased survival.[13] Bivariate analysis using the chi-square test (or Fischer exact if the data do not meet the requirements of the chi-square test) was performed to assess the relationship between diabetes mellitus and lung severity. The results of the analysis were considered significant if found a significance value (p) of <0.05. Data analysis was carried out using the Statistical Package for the Social Science (SPSS) version 22.0 program.

Ethical Approval was gained From RS Hasan Sadikin Bandung Ethics Committee No:LB.02.01/X.6.5/100/2022. This Study not involved human. The Data was from Medical record. The Data can be used after permission of head of Medical record Department.

3. Results

During the study period from January to May 2021, there were 538 subjects who met the inclusion criteria determined. A total of 387 (71.9%) subjects were aged less than 60 years with a greater number of women, namely 324 people (60.2%). Of all subjects, as many as 125 people had blood glucose levels above normal; 81 people were diagnosed with diabetes mellitus, while the remaining 44 people had reactive hyperglycemia. The characteristics of the subjects are presented in [Table 1]. In the examination of HbA1c levels, the average value in subjects with diabetes mellitus was 9.00 ± 1.77%. In subjects with reactive hyperglycemia, the median value was 5.85% with the lowest HbA1c level of 4.5% and the highest HbA1c level of 6.4% [Table 1].

Chest X-ray examination was performed on all patients. As a result, it was found that 357 of 538 subjects (66.4%) had lung abnormalities. Lung severity and its characteristics are presented in Table 2. The majority of the subjects had bilateral lung abnormalities with predominant areas in all lung fields, followed by middle and lower lung fields. In patients with diabetes mellitus, the predominant area is more in the middle and lower lung fields than in all lung fields. Lung involvement with an upper predominant area is the least common. The most common pulmonary pattern found was consolidation—with as many as 130 subjects (36.4%), followed by ground-glass opacity —with as many as 124 subjects (34.7%). The rest were reticular and nodular images—with as many as 82 subjects (23%) and 21 subjects (5.9%), respectively. Patients with diabetes mellitus had almost the same pulmonary pattern of consolidation, ground-glass opacity and reticular, with as many as 24, 21 and 21 people, respectively, whereas, in patients with reactive hyperglycemia, the most common pulmonary pattern found was ground-glass opacity. From all pulmonary patterns, as many as 15 people (4.2%) had pleural effusion. Lung severity was assessed using the BRIXIA score. Based on these scores, 461 subjects (85.7%) had a score of 0–10, and the remaining 77 subjects (14.3%) had a score of 11–18. Higher scores are associated with more severe lung severity. The BRIXIA score is presented in Table 1.

Table 3 shows the relationship between diabetes mellitus and lung severity as assessed by the chi-square test. The results obtained a non-significant relationship between diabetes mellitus as well as reactive hyperglycemia and lung severity degree, each with $p = 0.450$ and $p = 0.624$. When the chi-square test was carried out in the group aged 60 years and over, a significant relationship was found between diabetes mellitus and lung severity, with a p-value of 0.024.

4. Discussion

Pulmonary severity was assessed based on the BRIXIA score. The BRIXIA score determines lung involvement by dividing the lungs into six sections and each is assigned a score of 0, 1, 2, or 3 and the total obtained score is 0–18. The higher the score obtained, the more severe is the lung involved. In this study, the majority of subjects (85.7%) had a BRIXIA score of 0–10, while the remaining (14.3%) subjects had more severe degrees.

In addition to the BRIXIA score, lung severity radiographs can also be assessed using the RALE score and percentage of opacity. These three assessments can be done in a short time. A higher value indicates a greater degree of lung severity and is associated with the risk of intensive care unit admission and death.[13] In their study, Crooks and Card observed the severity of radiological features to predict the worsening and outcome of patients with COVID-19. In a study conducted in the UK during the February–July 2020 period, lung radiographs were examined and assessed using the BRIXIA score, RALE, and percentage of opacity. The results showed 751 lung radiographs, patients with opacity >75% had a median admission to the intensive care unit or death value within 1–2 days. In addition, the median survival value was found for the BRIXIA score category of 11–15 for 7.5 days and for the BRIXIA score category of 16–18 for 1.15 days.[13] Using two scoring methods, namely the BRIXIA score and percentage of opacity, Balbi et al. obtained similar results. In this study, it was stated that the use of the BRIXIA score can be used to predict mortality, while the percentage opacity score can be used to predict the need for ventilation assistance. A chest X-ray is a useful examination in assessing COVID-19 patients. Assessment of lung severity on X-rays needs to be integrated with other data such as patient history, PaO_2/FiO_2 ratio, and SpO_2 values to predict mortality and the need for ventilation assistance when patients come to the emergency department.[14]

Another study conducted by Maroldi et al. also assessed the role of lung X-rays in predicting the outcome of patients with pneumonia due to COVID-19. In this study, a BRIXIA score of 0–18 was used to assess pulmonary involvement. Of a total of 953 patients who met the criteria, it was found that higher scores were found more in patients who died than in patients who recovered. In statistical analysis, it was found that the BRIXIA score has a strong correlation with disease severity and outcome. The BRIXIA score along with the prognostic model is recommended to be used in predicting outcomes in COVID-19 patients.[15] Worse lung appearance was found more in male than female patients in the group of patients aged 50–79 years. This was found in a study by Borghesi et al. in Italy who evaluated the relationship of chest X-ray score with the age and sex of patients with COVID-19. The highest chest X-ray score (median 8) was found in men aged 50 years and older and women aged 80 years and older. These two groups are those with the highest risk for experiencing severe illness.[16]

In the study by Guan et al. on the clinical characteristics of COVID-19 patients in China, it was reported that ground-glass opacity was the most common finding in computed tomography (CT) chest radiographs. In 157 of 877 patients (17.9%) no chest radiographic abnormalities were found.[17] This is somewhat different from the results of this study which found consolidation as the most abundant pattern, followed by ground-glass opacity, which was close to the number. Patients without abnormalities on chest radiographs were reported in a higher number of 33.6% than in Guan et al. of 17.9%. The main difference in the two studies is the use of radiographic modalities where Guan et al. used a CT

scan while this study used a chest X-ray.

Diabetes mellitus is one of the factors that play a role in the outcome of patients with COVID-19.[8–11] Pazoki et al. investigated the mortality risk and severity of COVID-19 patients with diabetes mellitus. The results were obtained from 574 patients treated with COVID-19; 135 of the 176 patients with diabetes mellitus had severe conditions with a higher mortality rate of 30.7% than the non-diabetic patients with a mortality rate of 12.6%. Patients with diabetes mellitus who present with conditions of lower oxygen saturation, higher body temperature and higher blood urea levels are more prone to develop severe COVID-19 and have a poorer prognosis. In this study, the radiological features of the patient were not explained. However, 38.6% of patients with diabetes mellitus had acute respiratory distress syndrome (ARDS) and 19.3% of them required invasive ventilation.[18] A meta-analysis by Kumar et al. stated that diabetes mellitus in COVID-19 patients was associated with a twofold increase in mortality and severity of symptoms. In this study, several confounding factors for the risk of diabetes mellitus include old age, hypertension, the presence of cardiovascular disease and obesity that occur together with diabetes mellitus suffered by the patient.[8]

The condition of hyperglycemia, whether in patients diagnosed with diabetes mellitus or not, is thought to be associated with a more severe COVID-19 condition. This was stated by Iacobellis et al. who conducted an analysis of hyperglycemic conditions related to radiological predictors of patients with COVID-19. Acute hyperglycemia conditions can cause an inflammatory process and abnormal immune response. These contribute to the worsening and progression of the radiological features of ARDS in COVID-19 patients. Adequate management of hyperglycemia can contribute to the outcome of patients with COVID-19, whether or not they have diabetes mellitus.[12] In this study, it was found that diabetes mellitus was associated with a more severe degree of lung severity in patients aged $\geq$60 years. According to Dessie et al. old age is one of the factors that increase the risk of fatal outcomes. In addition, other factors are acute kidney failure, chronic obstructive pulmonary disease, hypertension, cardiovascular disease, diabetes mellitus, obesity and cancer.[19]

The relationship of lung severity with diabetes mellitus was previously reported in patients with tuberculosis infection. In their study, Barreda et al. stated that patients with hyperglycemia (both diabetes mellitus and prediabetes) had a more severe radiographic presentation and a number of pulmonary tuberculosis lesions. It was found that patients with hyperglycemia had more cavities, alveolar infiltrates and fibrosis than normoglycemic patients. The underlying mechanism is associated with a state of leukocyte hyperstimulation due to tuberculosis and hyperglycemia causing the process of 'premature aging' of the lungs.[20] The condition of acute hyperglycemia commonly suffered in patients with sepsis or trauma causes an increase in the inflammatory process; this is reported to exacerbate the damage suffered in patients with acute lung injury (ALI). Wu et al. found that, in ALI with hyperglycemia, severe lung injury occurred along with pulmonary edema, alveolar protein leakage and lung inflammation. This was not observed in the ALI model without hyperglycemia. The pulmonary injury occurs along with increased proinflammatory cytokines, infiltration of neutrophils and alveolar macrophages—and expression of pulmonary sodium-potassium-chloride co-transporter 1 (NKCC1).[21]

This study is the first study conducted in Indonesia to analyze the relationship between diabetes mellitus and lung severity in COVID-19 patients. Limitations in this study are the presence of confounding factors such as hypertension, obesity and cardiovascular disorders which were not taken into account. Therefore, further studies are needed with more complete data and larger sample size to ascertain the relationship between diabetes mellitus and hyperglycemia with lung severity.

5. Conclusion

There is a significant relationship between diabetes mellitus and lung severity in COVID-19 patients aged $\geq$60 years with bilateral lung involvement without pathognomonic pattern and BRIXIA score over 11. Chest X-rays have various advantages, such as: Faster to do, minimal cost and more availability in the emergency room compared to thorax CT scan. It also can be concluded that DM is not the only aggravating factors of the lung severity from this study. A geriatric category is needed in addition to comorbidities to obtain a severe degree.

Ethical approval and consent to participate

Ethical Approval was gained From RS Hasan Sadikin Bandung Ethics Committee No:LB.02.01/X.6.5/100/2022. This Study not involved human. The Data was from Medical record. The Data can be used after permission of head of Medical record Department.

Consent for publication

Not applicable.

Availability of data and materials

The authors declare that the data regarding this manuscript can be accessed as per the request of any interested body.

Funding

The authors received no specific funding for this work.

Authors contribution

AGC: wrote the proposal, participated in data collection, AGC, DKD, HGN and IHH analyzed the data, drafted the paper and prepared the manuscript, approved the proposal with few revisions, participated in data analysis and revised subsequent drafts of the paper. All the authors read and approved the final manuscript.

Declaration of competing interest

The authors declare no conflict of interest exists.

Acknowledgments

Our appreciation goes to Universitas Padjajaran dan Hasan Sadikin Hospital; for providing ethical.

clearance to carry out this study. We also would like to acknowledge the data collectors and study participants.

Appendixes

Table 1
Subject Characteristics, HbAIC Level and BRIXIA SCORE

Characteristics	N (%)
	N = 538
Age	
<60 years old	387 (71.9)
≥60 years old	151 (28.1)
Gender	
Male	214 (39.8)
Female	324 (60.2)
Diabetes mellitus	
Yes	81 (15.1)
Not	413 (76.8)
Hyperglycemia	44[2,8]
HbA1C levels in Subjects	Mean ± SD
Diabetes Mellitus (N = 81)	9.00 ± 1.77
Hyperglycemia (N = 44)	5.77 ± 0.45
BRIXIA score on subjects	Mean ± SD
Diabetes Mellitus (N = 81)	6.28 ± 4.56
Hyperglycemia (N = 44)	4.95 ± 4.36
Normal (N = 413)	4.30 ± 4.86

Table 2
Lung Conditions in Subjects based on the Presence of Diabetes Mellitus.

Characteristics	Diabetes mellitus		Reactive Hyperglycemia	Total
	Yes	Not		
Score (N=538)				
0–10	67	355	39	461
11–18	14	58	5	77
Lung Location (N=357)				
Bilateral	57	207	27	291
Right	8	37	8	53
Left	6	7	0	13
Predominant Area (N=357)				
Whole lung	26	111	17	154
Upper + middle	0	1	0	1
Upper + lower	0	1	1	2
Middle + lower	32	66	6	104
Upper	0	1	0	1
Middle	2	3	0	5
Lower	11	68	11	90
Pulmonary Pattern (N=357)				
Consolidation	24	95	11	130
Ground-glass opacity	21	89	14	124
Reticular	21	53	8	82
Nodular	5	14	2	21
Pleural Effusion (N=357)				
Yes	1	13	1	15
Bilateral	1	5	0	6
Right	0	3	1	4
Left	0	5	0	5
No	71	237	34	342

Table 3
Relationship between Diabetes Mellitus and Lung Severity

Age	Glycemic	BRIXIA scores		Total	p	OR (95% CI)
		0–10	11–18			
All ages (N = 538)	DM	67	14	81	0.450	
	Hyperglycemia	39	5	44	0.624	0.253 (0.07–0.90)
	Normal	355	58	413		
≥60 years (N = 151)	DM	32	3	35	0.024*	
	Hyperglycemia	14	2	16	0.351	3.95 (1.12–13.95)
	Normal	73	27	100		

DM = Diabetes Mellitus, OR= Odds Ratio, CI = Confidence Interval.
* Significant results, 'Using Fisher exact.

References

1 Lippi G, Sanchis-Gomar F, Henry BM. Coronavirus disease 2019 (COVID-19): the portrait of a perfect storm. *Ann Transl Med*. 2020;8, 497–497.
2 Anon Who. Coronavirus (COVID-19) dashboard | WHO coronavirus (COVID-19) dashboard with vaccination data. https://covid19.who.int/. Accessed January 12, 2022.
3 Anon. Peta sebaran | Covid 19.go.id. https://covid19.go.id/peta-sebaran. Accessed January 14, 2022.
4 Bajgain KT, Badal S, Bajgain BB, Santana MJ. Prevalence of comorbidities among individuals with COVID-19: a rapid review of current literature. *Am J Infect Control*. 2021;49:238–246.
5 Emami A, Javanmardi F, Pirbonyeh N, Akbari A. Prevalence of underlying diseases in hospitalized patients with COVID-19: a systematic review and meta-analysis. *Arch Acad Emerg Med*. 2020;8:1–14.
6 Gentile S, Strollo F, Ceriello A. COVID-19 infection in Italian people with diabetes: lessons learned for our future (an experience to be used). *Diabetes Res Clin Pract*. 2020;4, 108137.
7 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet (London, England)*. 2020;395:1054–1062.
8 Kumar A, Arora A, Sharma P, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. *Diabetes Metab Syndr Clin Res Rev*. 2020;14:535–545.
9 Aggarwal G, Lippi G, Lavie CJ, Henry BM, Sanchis-Gomar F. Diabetes mellitus association with coronavirus disease 2019 (COVID-19) severity and mortality: a pooled analysis. *J Diabetes*. 2020;12:851–855.
10 Zhang Y, Cui Y, Shen M, et al. Association of diabetes mellitus with disease severity and prognosis in COVID-19: a retrospective cohort study. *Diabetes Res Clin Pract*. 2020;165, 108227.
11 Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia – a systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr Clin Res Rev*. 2020;14:395–403.
12 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.
13 Au-Yong I, Higashi Y, Giannotti E, et al. Chest radiograph scoring alone or combined with other risk scores for predicting outcomes in COVID-19. *Radiology*. 2021, 210986.
14 Balbi M, Caroli A, Corsi A, et al. Chest X-ray for predicting mortality and the need for ventilatory support in COVID-19 patients presenting to the emergency department. *Eur Radiol*. 2021;31:1999–2012.
15 Maroldi R, Rondi P, Agazzi GM, Ravanelli M, Borghesi A, Farina D. Which role for chest x-ray score in predicting the outcome in COVID-19 pneumonia? *Eur Radiol*. 2021;31:4016–4022.
16 Borghesi A, Zigliani A, Masciullo R, et al. Radiographic severity index in COVID-19 pneumonia: relationship to age and sex in 783 Italian patients. *Radiol Medica*. 2020;125:461–464.
17 Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708–1720.
18 Pazoki M, Keykhaei M, Kafan S, et al. Risk indicators associated with in-hospital mortality and severity in patients with diabetes mellitus and confirmed or clinically suspected COVID-19. *J Diabetes Metab Disord*. 2021;20:59–69.
19 Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: a systematic review and meta-analysis of 42 studies and 423,117 patients. *BMC Infect Dis*. 2021:21.
20 Barreda NN, Arriaga MB, Aliaga JG, et al. Severe pulmonary radiological manifestations are associated with a distinct biochemical profile in blood of tuberculosis patients with dysglycemia. *BMC Infect Dis*. 2020;20:1–14.
21 Wu CP, Huang KL, Peng CK, Lan CC. Acute hyperglycemia aggravates lung injury via activation of the SGK1–NKCC1 pathway. *Int J Mol Sci*. 2020;21:4803, 2020;21:4803.