Radiograph Feature in COVID-19 Patients With Diabetes Mellitus At Dr. Soetomo Hospital Surabaya

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Abstract

Objectives : COVID-19 disease causes considerable morbidity and mortality. Older age and the presence of diabetes mellitus, hypertension and obesity significantly increase the risk of hospitalization and death in COVID-19 patients. COVID-19 patients with other comorbidities such as diabetes are at higher risk of developing severe pneumonia. Several studies have shown a higher susceptibility to several infectious diseases in people with diabetes, possibly due to an unregulated immune system. Plasma glucose levels and diabetes are independent predictors of mortality and morbidity in patients with SARS. Chest X-ray imaging plays an important role in both assessment of disease extent and follow-up, by knowing the pattern of chest radiography in patients with COVID-19 with Diabetes Mellitus, a radiologist can assist clinicians in predicting the progression of chest radiography in relation to blood glucose levels in patients.

Method : A descriptive study with a retrospective design was conducted on 134 patients with confirmed COVID-19 and diabetes mellitus who were admitted to Dr. Soetomo General Academic Hospital in 2020. Data on chest radiography and random blood glucose levels were obtained during the first 24 hours of treatment. We evaluated the lung disease based on features, distribution and location.

Result : The gender of COVID-19 patients who had the most Diabetes Mellitus was male (55.2%) with the highest age group being more than 50 years (70.8%) with the highest random glucose levels > 200 mg/dl (64.9%). The most radiographic features in COVID-19 patients with Diabetes Mellitus were consolidation/alveolar infiltrate both in patients with glucose level > 200 mg/dl (64.9%) or < 200 mg/dl (35.1%), with the most peripheral distribution (97,8%) and the most locations being a combination of the upper-middle-lower zone at right lung (81,3%) and left lung (70,9%)

Conclusion: Radiograph feature of COVID-19 patients with Diabetes Mellitus both in patients with glucose level > 200 mg/dl and < 200 mg/dl were mostly consolidation/alveolar infiltrate, with the most peripheral distribution and the most locations being a combination of the upper-middle-lower zone.

Keywords : COVID-19, Diabetes Mellitus, Radiograph, Chest X-Ray

Introduction

Infection with SARS-CoV-2, and the resulting COVID-19 pandemic, has led to a devastating rise in disability and death across the globe. The highest mortality rates have been in patients with concomitant diabetes mellitus, found in approximately 8% of COVID-19 cases, with a three-fold higher risk of death than those without this comorbidity [1,2]. High glucose concentrations in the blood impair the immune system and inflammatory response, and thus increase the rate of the disease's evolution, as shown by the pattern of chest radiographs and an increase in acute respiratory distress syndrome in COVID-19. Regardless of the patient's status of diabetes mellitus, a hyperglycemic state upon the initial infectious encounter with the virus is virtually the sole predictor of the chest X-ray features typical of COVID-19 [1,3].

Materials and Method

A descriptive study with a retrospective design was conducted with data from the medical records of 134 patients who met the inclusion criteria. All patients with COVID-19 confirmed by a polymerase chain reaction (PCR) test and a previous diagnosis of diabetes mellitus who were admitted to Dr. Soetomo General Academic Hospital during 2020 were included in the study. All participants underwent chest radiography using a Carestream DRX Revolution Mobile X-ray type K5807-8357, with raw data and random blood glucose levels obtained in the first 24 hours of treatment. Patients whose raw data were not recorded in the hospital's systems were excluded from the study.

The random blood glucose levels obtained were categorized as either < 200 mg/dl or > 200 mg/dl and then were evaluated the lung disease based on distribution, location and features of chest radiograph.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Medical Research Ethics Committee of Dr. Soetomo General Hospital, Surabaya, Indonesia. Prior to being included in the study, all participants gave their written informed consent to participate.

Result

The number of male patients in our study was 74 subjects (55,2%) and female (60 subjects (44,8%) with The highest age group being more than 50 years (70.8%) (Table1). And the highest random glucose levels between patients was > 200 mg/dl (64.9%) (Table 2).

Table 1. Characteristic of Sample Based on Gender and Age

	Characteristic Sample	Total Sample (n=134)
Gender	Male	74 (55,2)
	Female	60 (44,8)
Age	< 50	39 (29,1)
	>50	95 (70,8)

Table 2. Blood Glucose Level of Sample

Blood Glucose Level	Gender		Total Sample (n=134)
	Man	Woman	
< 200 mg/dl	29(21,6)	18 (13,4)	47 (35,1)
> 200 mg/dl	45(33,6)	42 (31,3)	87 (64,9)

The radiographic features observed include nodules, pleural effusions, interstitial infiltrates (reticular, reticulonodular and nodular) and alveolar infiltrates/consolidations. Assessment was carried out in each category of blood sugar < 200 mg/dl and > 200 mg/dl. The most radiographic features in COVID-19 patients with Diabetes Mellitus were consolidation/alveolar infiltrate both in patients with glucose level > 200 mg/dl (64.9%) or < 200 mg/dl (35.1%) (Table 3).

Table 3. Radiograph Features of Patients COVID-19 with DM

Radiographic features	Blood Glucose Level (n=134)	
	> 200 mg/dl	< 200 mg/dl
Nodul	2 (1,5)	1 (0,7)
Pleura Efussion	7 (5,2)	8 (5,9)
Interstisial Infiltrate :		
- Retticular	36 (26,9)	18 (13,4)
- Retticulonodular	35 (26,1)	26 (19,4)
- Nodular	-	-
Alveolar Infiltrate / konsolidasi	72 (53,7)	42 (31,3)

The most lung disease distribution was peripheral distribution (97,8%) (Table 4) and the most locations being a combination of the upper-middle-lower zone at right lung (81,3%) and left lung (70,9%) (Table 5).

Table 4. Distribution of Radiograph Features Patients COVID-19 with DM

Distribution	**Blood Glucose Level (n=134)**	
	> 200 mg/dl	< 200 mg/dl
Perifer	84 (62,7)	47 (35,1)
Central	13 (9,7)	2 (1,5)
Perifer and Central	11 (8,2)	2 (1,5)

Table 5. Location of Radiograph Features Patients COVID-19 with DM

Location	**Right Lung**	**Left Lung**
Upper Zone	1 (0,7)	-
Mid Zone	-	3 (2,2)
Lower Zone	2 (1,5)	5 (3,7)
Upper and Mid Zone	2 (1,5)	1 (0,7)
Upper and Lower Zone	-	-
Mid and Lower Zone	19 (14,2)	29 (21,6)
Upper-Mid-Lower Zone	109 (81,3)	95 (70,9)

Discussion

The study was conducted on 134 research subjects of COVID-19 pneumonia patients who had DM comorbidities who met the inclusion and exclusion criteria. Age range of research subjects between 20-79 years, with an average age of 40 years. The highest age group being more than 50 years with a total of 55 people (41.4%). According to a literature review by Roziqo, et al (2021) which states that patients aged > 50 years have higher expression of ACE-2 which is encoded by the ACE-2 gene and other conventional factors, for example reduced immune system, decreased organ function or the presence of comorbidities that increase the risk of death[18].

The increased expression of ACE 2 that occurs in DM patients can also support more efficient cell binding and then make it easier for the virus to enter cells[14]. In this study, the number of male subjects was 74 people (55.2%) which was more than the female subjects. According to a literature review by Roziqo, et al (2021) that male sex patients have higher ACE-2 expression which is regulated by male sex hormones, thereby making male more at risk of being infected with SARS-CoV-2. Another hypothesis states that female can resist the development of SARS-CoV-2 infection, because they carry X-linked heterozygous alleles called sex dimorphism [18].

The study showed that COVIV-19 patiens with Diabetes Mellitus which have blood glucose plasma < 200 mg/dl were 27 (20.1%) male patients and 17 (12.7%) female patients with a total of 44 patients. (32.8%), and blood glucose plasma > 200 mg/dl were 47 (35.1%) male patients and 43 (32.1%) female patients with a total of 90 patients (67.2%). Oliviera et al (2020) stated that high blood sugar levels are associated in parallel with the expression of IL-1β and other pro-inflammatory cytokines such as TNF-α, IL-6, and IFN-α, IFN-β, and IFN-λ [9] This cytokine plays an important role in cytokine storms and lung injury in COVID-19 patients. Acute hyperglycemia can lead to abnormalities in inflammatory and immune responses thereby contributing to the development and progression of radiographic findings of ARDS in COVID-19 [1]. In a study conducted by Muniyappa, et al (2020) it was said that the increased expression of ACE 2 that occurs in DM patients can support more efficient cell binding and then make it easier to enter the cell. Early initiation of neutrophil and macrophage function is impaired in DM.

Characteristics based on radiological features observed in this study included nodules, pleural effusions, interstitial infiltrates (reticular, reticulonodular, nodular) and alveolar infiltrates/ consolidations. In the present study, the predominant radiological features were alveolar infiltrates. The systemic inflammatory reaction causes the lungs to produce mucus and surfactant, then the inflammatory exudate peripherally fills the alveoli and spreads to all segments through the pores of the conjunctiva so that it closes the ciliary cells where on chest radiographs it is shown that consolidation can fill the interstitium or alvaeolar space [14].

Moreover, a large body of evidence has suggested that the glucose metabolism pathway in the lung parenchyma is strongly associated with pathogen proliferation, inflammatory response, oxidative stress, and prothrombotic mechanisms, which contribute to the severity of disease. It has been found that glucose molecules in the airway surface liquid (ASL) are remarkably more concentrated in patients with diabetes, along with ASL accumulation in the alveolar space, substantial generation of reactive oxygen species (ROS), and the release of inflammatory cytokines, due to the impairment of SGLT-1 glucose reuptake. [9,10] Moreover, the high concentration of glucose in the ASL increases osmotic pressure within the alveolar space, leading to an increase in water content in the alveoli [9,10].

In this study the most common locations were the middle-lower zone combination and the upper-middle-lower zone combination, both on the right and left lung. It was also found that 131 people (97.8%) showed a dominant distribution of radiological images in the periphery and 15 people (9.7%) showed a dominant perihilar (central) distribution. The clinical manifestation and radiographic findings were highly influenced by the type of pathogen, as well as the patient's age and immune status [5]. The alveoli are typically covered by two types of pneumocytes; type 1 constitutes virtually the entire alveoli surface (about 95%), whereas type 2 pneumocytes are responsible for secreting surfactant, which improves the compliance of alveoli surfaces, and inhibits expiratory collapse of the alveoli. SARS-CoV-2 infects the alveoli with a tendency to invade type 2 pneumocytes rather than type 1. Interestingly, the virus tends to reach the most distal region of the respiratory tract, thereby infecting the peripheral and subpleural alveoli [6–8].

According to the British Society of Thoracic Imaging (BSTI) the Classic / Probable COVID-19 pattern category is when multiple opacity is found predominantly in the periphery and base of both lungs. Type 1 pneumocytes cover about 95% of the total surface area of the alveoli. Type 2 pneumocytes produce surfactant which is useful for reducing surface tension and preventing alveoli collapse during expiration. The virus can reach the gas exchange unit and infect type II alveolar cells compared to type I. The infected alveolar units tend to be peripheral and subpleural according to the location of the alveoli which are distal to the respiratory tract [6]. Diabetes is associated with higher ASL (Airway surface liquid) glucose concentrations, volume accumulation of ASL in the alveolar space, ROS (Reactive Oxygen Species) imbalance, and production of inflammatory chemokines. Under hyperglycemic conditions, increased glucose transport from plasma to ASL is not offset by the parallel adjustment by SGLT1-mediated glucose re-uptake, which explains the higher ASL glucose concentrations in the distal lung. Given the osmotic effect due to the high concentration of ASL glucose, this change may explain the higher total water content in the alveolar space during hyperglycemic conditions [9].

Conclusion

Radiograph feature of COVID-19 patients with Diabetes Mellitus both in patients with glucose level > 200 mg/dl and < 200 mg/dl were mostly consolidation/alveolar infiltrate, with the most peripheral distribution and the most locations being a combination of the upper-middle-lower zone.

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Conflict of Interest

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