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Research Article

Clinical, Radiological Features and Outcome of COVID-19 Patients in a Secondary Hospital in Jakarta, Indonesia

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ABSTRACT

Background: Amount of people infected with SARS-CoV-2 in Indonesia especially in Jakarta as the epicenter continues to rise. Limited published clinical data, scarcity and long turn over time of diagnostic testing put clinician, especially in primary and secondary hospital setting, in dilemma to make assessment and diagnosis. Our hospital (Budhi Asih Hospital) is a secondary referral hospital in East Jakarta has been designated for isolation and management of suspected and confirmed cases of COVID-19.

Objective: We try to describe the clinical, radiological and outcome features of COVID-19 in our hospital in order to help clinician make appropriate assessment within the setting of limited resources of a secondary referral hospital.

Methods: This is an observational case series study from confirmed COVID-19 patient in our hospital from first case admission on March 17, 2020 to April 30, 2020. We collected patient's demography, symptoms, exposure history, comorbidities, therapy, outcome, laboratory, chest x-ray and ECG consecutively. This study has been approved by our hospital ethics committee (No.47/KEP-ETIK/IV/2020).

Results: From March 17, 2020 to April 30 2020, there were 30 confirmed COVID-19 cases, 16 (53.3%) were male. Clinical symptoms were dyspnea in 22 (73.3%) and dry cough 16 (53.3%). Comorbidities were diabetes in 14 (46.6%), hypertension 10 (33.3%) and Coronary Artery Disease (CAD) in 10 (33.3%) patients respectively. Laboratory findings showed lymphopenia in 21 (70%) patients, increased inflammation marker in Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and Lactate Dehydrogenase (LDH) 21 (70%), 23 (76.6%) and 12 (40%) patients respectively. Twenty-seven (90%) cases had abnormal Chest X-Ray(CXR) and mostly severe18(60%). Descriptive finding for images included consolidation 16(53.3%) and Ground Glass Opacities (GGO) in 10 (33.3%) patients. Of 18 patients who underwent Electrocardiogram (ECG), abnormal ECG were found in 13 (72%) of them.

Conclusion: Based on our findings, most cases of COVID-19 admitted in secondary referral hospital were already in moderate to severe stages. This is most likely due to late referral from primary care and unspecific clinical features resemblance of other infectious diseases such as dengue, typhoid fever or other influenza. Inflammation marker, Neutrophil-to-lymphocyte ratio (NLR) and CXR are cost effective findings and can be used as a disease severity

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marker in primary health care to determine further referral. Furthermore, since cardiac dysfunction are also present in most cases, this warrant further investigation. Public awareness of signs, symptoms, early diagnostic testing protocols and case findings were important to reduce severity of diseases.

Keywords: Diagnosis; Covid-19; Limited resources

INTRODUCTION

A new emerging infectious disease which was first identified in Wuhan, China in late December 2019 goes on to cause a global pandemic worldwide. This disease is caused by a single RNA stranded, novel betacorona virus which was very similar with SARS-CoV and MERS-CoV in terms of binding receptor and belong to the same genus. The International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2 on February 11, 2020 and the disease was referred as COVID-19 by World Health Organization (WHO).The virus continues to threaten across the globe as more than 5,000,000 people were infected with more than 350,000 deaths [1,2].

Previous data from several countries indicated that the symptom of COVID-19 was fever, dry cough and fatigue. Other symptom includes myalgia, sore throat, dyspepsia, diarrhea, dyspnea and vomiting [3]. The clinical spectrum of COVID-19 can be ranging from asymptomatic, mild, moderate to severe disease that lead to severe respiratory distress. Indonesia is one of many countries impacted by this SARS-CoV-2 infection, as the first case was reported on March 2, 2020, and increased exponentially since then. As of May 24, 2020there were 22, 271 confirmed cases. Data from Republic of Indonesia Ministry of Health as of May 24, 2020 there were 6, 561 confirmed COVID-19 cases, with 505 deaths in Jakarta [4]. Our hospital, Budhi Asih, is one of secondary hospital located in East Jakarta, with a total capacity of 50beds for COVID-19.

Currently, there are no data available regarding the clinical characteristic of COVID-19 patient admitted in secondary hospital. This situation has put clinician in a dilemma on how to recognize, diagnose and when to treat the patients. The current diagnostic process for COVID-19 has some limitations, especially on the limited resources for Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) of SARS-CoV-2. Previously in Jakarta, there was only one central laboratory appointed to handle RT-PCR examination, thus turn over time can be overwhelmed.

MATERIALS AND METHODS

Study design and participants

This is a single center observational case series study. Data were collected consecutively during admission. The enrollment included from the first patient admitted to Emergency Department (ED) on March 17, 2020 until April 30, 2020. All 30cases enrolled in this study were confirmed COVID-19 from RT-PCR detection of SARS-CoV-2 using nasopharyngeal swab in line with guideline according to the diagnostic criteria by the Indonesian Ministry of Health. This study has been approved by Budhi Asih Hospital ethics committee (No.47/KEP-ETIK/IV/2020).

Data collection

Clinical characteristic, comorbidities, symptoms, laboratory, chest imaging as well as ECG changes were obtained consecutively during patients visit to the Emergency Department (ED). Treatments during hospitalization, referral, discharges and deaths were also recorded. All CXR were interpreted by local radiologist and have been reviewed by an external radiologist having 12 years experiences as a thoracic radiologist. To quantify the extent of infection, a severity score was calculated by adapting and simplifying the Radiographic Assessment of Lung Edema (RALE) score proposed by Warren et al and British Society of Thoracic Imaging (BSTI). Mild disease means 0-25% lung abnormality, moderate means>25%-50% and sever>50% respectively [5,6].

Statistical analysis

Variables were reported as frequency, percentages (%), mean (SD) if they are normally distributed and median with range (min-max) for abnormal distribution. Laboratory results are mentioned as actual data and assessed whether or not the measurements fell within normal ranges. Comparisons of percentages between groups displayed with Fischer's exact test. All data analysis was carried out using IBM SPSS statistics (Version 23).

RESULTS

Patient characteristics

Thirty confirmed COVID-19 patients were enrolled with mean age 53.9 ± 16.4 years, shown in Table 1, 16 (53.3%) were male and 14 (46.6%) were female.

Table 1: Clinical characteristics of patients with COVID-19.

Clinical characteristics	n=30 (%), mean+SD, median (min-max)
Age (year)	53.9+16.4
Sex	
Male	16 (53.3)
Female	14 (46.6)
Contact exposure	6 (20)

Smoker/former smoker	14 (46.6)
Symptoms	
Cough	16 (53.3)
Shortness of breath	22 (73.3)
Fever	10 (33.3)
Fatigue	10 (33.3)
Vomitting	5 (16.6)
Anosmia	2 (6.6)
Comorbid	
Diabetes Melitus	14 (46.6)
Hypertension	10 (33.3)
Coronary arterial disease Therapy	10 (33.3)
Antiviral	
Oseltamivir	23 (76.6)
Antibiotics	
Levofloxacin	6 (20)
Azithromycin	23 (76.6)
Others	
Chloroquine	22 (73.3)
Oxygen therapy	
Low flow oxygen therapy	19 (63.3)
Venturi mask	11 (36.6)
Length of stay (days)	4 (1-12)
Outcome	
Discharge	12 (40)
Referred	11 (36.6)
Death	7 (23.3)
Cause of death	
Respiratory failure	5 (16.6)
Septic shock	1 (7.7)
Malignant arrhythmia	1 (3.8)

Six patients (20%) had a history of contact exposure from various known cluster sites including family and religious gathering. Smoking history was found in 14 (46.6%) patients. Smoking history is considered important data, due to evidence that suggest smoking increase susceptibility to SARS-CoV-2 infection and may progress to severe disease due to increase of ACE2 receptors and underlying lung diseases [4]. Symptoms presented upon admission were dry cough 16 (53.3%) and shortness of breath 22 (73.3%) patients. Other symptoms that patients reported are fever 10 (33.37%), fatigue 10 (33.37%), vomiting 5 (16.6%) and anosmia 2 (6.6%) patients respectively. Comorbidities of these patients were diabetes in 14 (46.6%), hypertension 10(33.3%) and CAD 10 (33.3%) patients respectively.

Laboratory findings

Upon admission, 5 (16.7%) and 3 (10%) patients had a white blood cell count above and under normal range respectively, with mean value7.5+3.8 × 10^3/μL. Twenty-patients (66.7%) and only 1 (3.3%) and had neutrophils above and below normal range respectively. Twenty-one (70%) had lymphocytes count below normal range. Eosinophil count drop below normal range in 24 (80%) patients. Platelet counts below and above normal range were noted in 3 (10%) and 1 (3.3%) patients respectively. Neutrophil Lymphocyte Ratio (NLR) marker increased above normal in 19 (63.3%) patients. Hemoglobin level decreased in 9 (30%) patients. Inflammation marker such as Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP) and Lactate Dehydrogenase (LDH) were also measured and all values are shown to be increase dramatically. Twenty-one (70%), 23 (76.6%), 12 (40%) of ESR, CRP and LDHare above normal range respectively. Fourteen (46.6%) patients had elevated liver enzyme. Regarding blood gas analysis we recorded Partial Pressure of Arterial Oxygen (PaO_2) divided by Fraction of Inspired Oxygen (FiO_2) and Oxygen Saturation (SaO_2) with12 (40%) and 9 (30%) patients decrease below normal value respectively, shown in Table 2.

Table 2: Laboratory findings of COVID-19 patients on admission to hospital.

Clinical characteristics	**n=30 (%), mean+SD, median (min-max)**
White blood cell count; x 103/uL; normal range 3.8-10.6	7.5+ 3.8
Increase	5 (16.7)

Decrease	3 (10)
Neutrophilpercentage; normal range 50-70	76.8+7.7
Increase	20 (76.9)
Decrease	1 (3.8)
Neutrophil/Lymphocyte Ratio (NLR)	6.4 (2.8-30)
Increase	19 (63.3)
Lymphocytes percentage; normal range 25-40	13+6.4
Increase	0 (0)
Decrease	21 (70)
Eosinophils percentage; normal range 2-4	0 (0-3)
Increase	0
Decrease	24 (80)
Basophils percentage; normal range 0-1	0 (0-1)
Increase	7 (23.3)
Decrease	19 (63.3)
Monocyte percentage; normal range 2-8	7 (3-21)
Increase	10 (33.3)
Decrease	0
Platelet count; × 10^3/uL; normal range 150-440	215+101
Increase	1 (3.3)
Decrease	3 (10)
Hemoglobin; g/dL; normal range 13.2-17.3	13.4+2
Decrease	9 (30)
Erythrocyte sedimentation rate; mm/hour; normal range 0-30	62.6+ 39.8
Increase	21 (70)
C-reactive protein; mg/L; normal range<5	103 (5-120)
Increase	23 (76.6)
Lactate dehydrogenase; U/L; normal range<480	971.3+603.1
Increase	12 (40)
Alanine aminotransferase; U/L; normal range<34	53 (14-208)
Increase	14 (46.6)

PaO_2/FiO_2; normal range>250	327+129
Decrease	12 (40)
O_2 Saturation;%; normal range 95-100	96 (79-99)
Decrease	9 (30)

Sex is homogenous in proportion, we then try to compare percentages of severity between the groups but it was not statistically significant, shown in Table 3.

Table 3: Comparison between sex, lymphocyte with severity of CXR.

	Radiology severity		
Variable	**Mild-Moderate**	**Severe**	**Chi x^2 P (value)***
Sex			
Male	7 (43.8)	9 (56.2)	0,317
Feemale	4 (28.6)	10 (71.4)	
Lymphocyte			
Increased	4 (28.6)	10 (71.4)	0,47
Normal-decreased	7 (43.8)	9 (56.2)	
Note: *Fisher's test			

Chest X-ray findings

All patients underwent CXR examination upon admission in our ED due to practicality and availability, shown in Figure 1 of the 30 CXR included in this report only 3 (10%) patients were mild,9 (30%) was moderate while most of them 18(60%) was classified as severe.

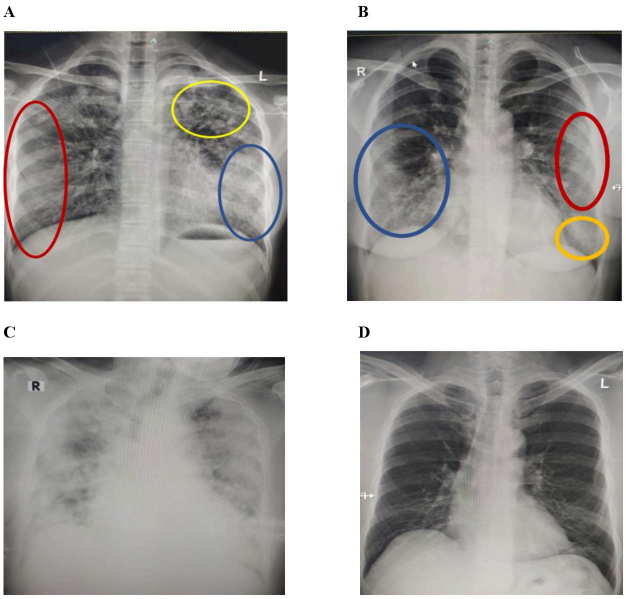

Figure 1: (A) CXR of a 55 year-old male showed right, middle and lower sub pleural consolidation (red), left lower consolidation (blue) and homogenous consolidation and reticulo-nodular opacity (yellow). (B) 37 year-old female with sub-pleural right lower zone GGO extend to paracardial (blue) and sub-pleural left middle and lower lung GGO (red and yellow). (C) 73 years old female with sub-pleural consolidation both of lung zone multi focal spread to para-cardial and peri-hilar with cardiomegaly showing severe typical covid-19. (D) 44 years old female with symptom only anosmia showed normal CXR.

Consolidation and GGO were the most common descriptive findings with 16(53.3%) and 10 (33.3%) respectively. Location of the abnormality was peripheral 19(63.3%) and bilateral in 22(73.3%)patients respectively. Nodule, effusion and reticular opacity were found to be uncommon. Interestingly enough we found cardiomegaly in 10(33.3%) which may be related to hypertension as comorbid, shown in Table 4.

Table 4: Characteristics of radiological findings of COVID-19 patients.

Radiologic patterns	**Categories**	**n=30 (% of total)**
Type of abnormality	Interstitial	2 (6.67)
	Ground glass opacities	10 (33.3)
	Consolidation	16 (53.3)

Severity	Mild	3 (10)
	Moderate	9 (30)
	Severe	18 (60)
Focality	Multifocal	16 (53.3)
Laterality	Bilateral	22 (73.3)
Centrality	Peripheral	19 (63.3)
	Central	2 (6.67)
Other	Cardiomegaly	10 (33.3)
	Nodules	2 (6.67)
	Reticular opacity	5 (16.67)
	Pleural effusion	1 (3.3)

ECG findings

From 30 patients, only 18 patients underwent ECG on the time of admission. One patients (5.56%) presented with supraventricular tachycardia and 17 (94.4%) patients had sinus rhythm. Most cases had tachycardia at admission with enlarged Left Atrial (LA) 9 (50%). Left and right ventricular hypertrophy was only found in 1 (5.56%) case each. Ten (55.55%) of the baseline ECG in this study showed ischemic sign, with the most frequent findings was T inversion in 6 (33.33%) followed by Q pathologic 3 (16.67%), ST depression 3 (16.67%), and ST elevation 1 (5.56%) respectively. There was only 1 (5.56%) case which had bundle branch block pattern (RBBB). We found that 5 (27.78%) had prolong QT interval (QTc>460 ms), shown in Table 5.

Table 5: Electrocardiography findings of COVID-19 patients.

Categories	Sub-categories	n=18 (% of total)
Rhythm	Sinus	17(94.4)
	SVT	1 (5.56)
Rate	Tachycardia	9 (50)
	Normal	9(50)
Axis	Normal	14 (77.77)
	LAD	3(16.67)
	RAD	1 (5.56)
PR interval	Prolong (≥ 200)	0 (0.00)
	Normal (<200)	18 (100)
Atrial Enlargement	LAE	9 (50)
	RAE	2 (11.11)
Ventricular Hypertrophy	LVH	1 (5.56)
	RVH	1 (5.56)
Bundle Branch Block	LBBB	0 (0.00)
	RBBB	1 (5.56)
Ischemic Sign	Total with ischemic sign	10 (55.55)
	T inverted	6 (33.33)
	ST depression	3 (16.67)
	ST elevation	1 (5.56)
	Q pathologic	3 (16.67)
QTC interval	Prolong (≥ 460 ms)	5 (27.78)
	Normal (<460 ms)	13 (72.22)

DISCUSSION

In this observational case series study, we reported and provided clinical and radiological features of COVID-19 in a secondary referral hospital in Jakarta. To our knowledge there has not been any published paper describing patients in the Indonesian capital city of Jakarta. Multiple factors such as limited, long turn over period of testing and symptoms resemblance of common tropical disease like dengue and typhoid fever resulted in delayed decision making by the clinician to make a timely intervention to reduce mortality. We hope that this early report could help clinician gain insight of which features may lead to high suspicion of COVID-19 cases and treat them promptly especially in area with limited resources.

Average age during admission was 53 years. Both male and female patient share same risk to COVID-19 infection. Despite other study that shows men are more susceptible to COVID-19 than female. There are no clear explanation regarding genetic or sex-specific effect. Several studies have shown that the severity and mortality with COVID-19 are related to age and comorbidities including diabetes, hypertension, cardiovascular and cerebrovascular disease. The symptoms of COVID-19 are similar to other viral upper respiratory illness which include fever, cough, fatigue and shortness of breath [7,8]. As indicated in many reports, we found that common symptoms dominated by cough, shortness of breath and fever, with uncommon

presentation including vomiting and anosmia. Patients exhibiting mild to severe conditions may share the same symptoms and required further observation and management [9].

Major laboratory markers were tracked from patient illness onset, whereas white blood cell count value in the majority of patients were found to be normal with differential low lymphocyte count. Lymphocyte play an important role in maintaining immune homeostasis and inflammatory response. A low lymphocyte count that is less than 20% is a reliable indicator of severity and hospitalization in COVID-19 patient. While it is found that multiple mechanisms might cause lymphopenia, this require further research to confirm [10].Previous studies has showed a depletion of CD8 T cells and dramatic loss of CD4 found in comparison to the healthy control group. Significant reduction of the CD8 and CD4 T Cells are also found in severe and critical COVID-19 patients [7,11,12]. Baseline lymphocyte count was lowest at early onset during hospitalization was found to be similar with other studies in China [13]. Interestingly monocyte count were found to be increased in 10 (38.5%) patients.

Current data have demonstrated a possible multiple organ failure in patients with COVID-19.Laboratory parameters that were documented have shown hepatic insufficiency elevation of Alanine aminotransferase (ALT). CRP, LDH and ESR elevations are consistent with previous reports in patients withCOVID-19. CRP is a systemic marker of acute-phase response in inflammation, infection and tissue damage. ESR is a non-specific inflammatory marker mainly reflects the change of plasma protein. However, role of inflammatory markers in monitoring the severity of COVID-19 is still controversial [14,15]. Research suggests that these abnormalities maybe related to the cytokine storm in viral infection. These data indicated that progressive immune-associated injury and inadequate adaptive immune responses could be possible mechanisms by which SARS-CoV-2 causes severe illness and fatal outcomes [16]. Value of NLR and Lymphocyte-to-C-reactive protein ratio (LCR) were cost effective to help clinical prognosis and diseases severity [17].

Marker for Acute Respiratory Distress Syndrome (ARDS), reduction of PaO_2 and ratio of PaO_2/FiO_2 of 12 (46.2%) patients and 9 (34.2%) decrease below normal value, can be explained due to disease severity based on CXR and NLR. The majority of deceased patient have shown to have SaO_2 less than 95% during admission indicating early sign of respiratory impairment [8].

CXR examination showed that most patients presented in moderate to severe stages, with only 3 (10%) mild cases. This finding suggested widespread transmission within community being under detected therefore close contact should be traced and tested. Descriptive findings such as large GGO, consolidation, bilateral and multifocal finding were consistent with progressive and peak stages of the disease. Our results suggest that CXR plays an important role in initial screening for suspected COVID-19 patient and may obviate the need for a chest Computed Tomography (CT), thus reducing burden on CT used in this pandemic. The mild abnormality initially was not caught by our first radiologist because its subtle appearance located in the lung peripheral and should have been followed by chest CT in referral hospital. Radiologist should pay more attention to find small GGO in the early and mild disease. A study reported that the most common finding was peripheral rounded consolidation, GGO and the imaging changes peaked at day 10-12 from symptom onset [18]. Recent study from the urgent care medicine in the United State of America (USA) with 636 CXR involved show relatively different results. They found that GGO and interstitial changes as the predominant findings indicating the disease was early and mild [19].

Cardiac involvement is prevalent and prognostic in COVID-19 and could possibly impair cardiac functions by causing cardiac injury through direct infection (through ACE2 receptor binding and up regulation of ACE2) or cardiac stress due to hypoxemia. Binding of SARS CoV-2 also occur through CD209 in macrophages, which promote virus invasion to cardiac and vascular tissues. COVID 19 infection could also induce plaque rupture resulting in type 1 myocardial infarction. It is also known that underlying heart disease increases the possibility of patient to contract COVID-19 and furthermore jeopardize the condition for the infected patient [20,21].

In this study, we observe most of the positive COVID-19 patient presented with ischemic sign on their baseline ECG. Half of the presented ECG showed tachycardia, which were suggested due to other related symptoms such as fever, pain, and shortness of breath.

It is also shown that half of the presented ECG in this study have left atrial (LA) enlargement that is related to CAD risk factors such as chronic hypertension. In this study, five of ten patients with ischemic sign on ECG were categorized in severe group. The expression of mediators due to that condition could lead to cytokine release that may worsen the severity of SARS-CoV-2 infection. This finding was considered parallel with previous statement of European Society of Cardiology that in the group of patient who died from corona virus, 10.6% had CAD [21]. The limitations of this study included a single center in a secondary hospital observational design; the small number of confirmed cases of COVID-19 and incomplete ECG data may limit the interpretation and the clinical relevance of our data. Hence, there has yet any data published in this concern.

CONCLUSION

Based on our findings, most cases of COVID-19 admitted in secondary referral hospital were already in moderate to severe stages. This is most likely due to late referral from primary care and unspecific clinical features resemblance of other infectious diseases such as dengue, typhoid fever or other influenza. Inflammation marker, Neutrophil-to-lymphocyte ratio (NLR) and CXR are cost effective findings and can be used as a disease severity marker in primary health care to determine further referral. Furthermore, since cardiac dysfunction are also present in most cases, this warrant further investigation. Public awareness of signs, symptoms, early diagnostic testing protocols and case findings were important to reduce severity of diseases.

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