Coronavirus Pandemic

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

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Abstract

Introduction: The numbers of people infected with SARS-CoV-2 in Indonesia especially in Jakarta as the epicenter continue to rise. Limited published clinical data, scarcity and long turn over time of diagnostic testing put clinician in dilemma to make diagnosis.

Methodology: This is an observational case series study from confirmed COVID-19 patient in our hospital from first case admission on 17 March 30 April, 2020. We collected patient’s demography, symptoms, comorbidities, therapy, laboratory, chest x-ray and ECG consecutively.

Results: Between 17 March 2020 and 30 April 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 severe 18 (60%). Descriptive finding for images included consolidation 16 (53.3%) and Ground Glass Opacities (GGO) in 10 (33.3%) patients.

Conclusions: 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. Inflammation marker and CXR are cost effective findings and can be used as marker to determine further referral.

Key words: Diagnosis; Covid-19; Limited resources.

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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 beta corona 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 11 February 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 symptoms of COVID-19 were fever, dry cough and fatigue. Other symptoms include 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 24 May 2020 there 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 [corona.jakarta.go.id],[4] Our hospital, Budhi Asih, is one of secondary hospital located in East Jakarta, with a total capacity of 50 beds 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 have 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.

**Methodology**

**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 17 March 2020 until 30 April 2020. All 30 cases 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 severe > 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 were 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 (Table 1), 16 (53.3%) were male and 14 (46.6%) were female. 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 are 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 value $7.5 + 3.8 \times 10^9/\mu$L. 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. Hemoglobin level decreased in 9 (30%) patients. Neutrophil/Lymphocyte Ratio (NLR) marker increased above normal in 19 (63.3%) 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-patients (66.7%), 23 (76.6%), 12 (40%) of ESR, CRP and LDH were also measured and all values are shown to be increase dramatically. Twenty-patients (66.7%) and only 1 (3.3%) had neutrophils above and below normal range respectively. Neutrophil/Lymphocyte Ratio (NLR) marker increased above normal in 19 (63.3%) patients.

**Chest X-ray findings**

All patients underwent CXR examination upon admission in our ED due to practicality and availability (Figure 1). Of the thirty 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. 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 (Table 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.

**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 10^9/µL; normal range 3.8 - 10.6 | 7.5 ± 3.8 |
| Increase | 5 (16.7) |
| Decrease | 3 (10) |
| Neutrophil percentage; normal range 50 - 70 | 76.8 ± 7.7 |
| Increase | 20 (69.9) |
| 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; x 10^3/µL; 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) |
| PaO2/FiO2; normal range > 250 | 327 ± 129 |
| Decrease | 12 (40) |
| O2 Saturation; %; normal range 95-100 | 96 (79-99) |
| Decrease | 9 (30) |
Table 3. Characteristics of radiological findings of COVID-19 patients.

| Radiologic patterns       | Categories                  | N  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)                |

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 para cardiac (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.
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) (Table 4).

**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 gender-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]. Gender is homogenous in proportion, we then try to compare percentages of severity between the groups but it was not statistically significant. (Table 5)

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 homestasis 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 of the

| 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)         |
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 hospitalisation 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 with COVID-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 may be 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].

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

| Variable        | Radiology severity | χ² | p (value)* |
|-----------------|--------------------|----|-----------|
|                 | Mild-Moderate      |    |           |
| Gender          |                    |    |           |
| Male            | 7 (43.8)           |    |           |
| Female          | 4 (28.6)           |    |           |
| Lymphocyte      |                    |    |           |
| Increased       | 4 (28.6)           |    |           |
| Normal-decreased| 7 (43.8)           |    |           |

*p (value)* Fisher’s test.

Table 5. Comparison between sex, lymphocyte with severity of CXR.
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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