

Asymptomatic and Minimally Symptomatic COVID-19 in Medical Frontliners: A Case Series from National Cardiovascular Centre Harapan Kita Indonesia

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ABSTRACT COVID-19 has widely spread in Indonesia and threatened health care workers at the frontline. We reported 12 cases of COVID-19 via local transmission among cardiology residents in National Cardiovascular Centre Harapan Kita Indonesia. All cases were asymptomatic or minimally symptomatic. Universal precaution and standardized protective equipment have been used but still ineffective to prevent bacterial transmission. Improper doffing technique and unfitted protective equipment might be responsible for cross-infection.

KEYWORDS COVID-19, asymptomatic infections, personal protective equipment, Indonesia

Introduction

In recent months Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has been causing a worldwide pandemic of Coronavirus disease 2019 (COVID-19). Mode of transmission is via droplet, direct or indirect contact, and possible airborne transmission in aerosol-generating procedures [1, 2]. The clinical manifestation itself is heterogeneous: some patients are critically ill while some are minimally symptomatic or even asymptomatic [3].

The first case of COVID-19 in Indonesia was reported on March 2, 2020, in Jakarta [4]. By the end of May, the disease has reached 20796 cases in 34 provinces of Indonesia with a case fatality rate at 6.4% (1326 deaths) [5]. The diagnosis and management of COVID-19 in Indonesia are troubled by a minuscule number of gold-standard test (virus sequence detection with reverse transcription-polymerase chain reaction/RT-PCR),

poor compliance toward social distancing policy, and limited availability of personal protective equipment (PPE) [6, 7]. These limitations may potentially cause underdiagnosis, intractable viral transmission, and increased risk of infection in health care workers. We report 12 positive cases of COVID-19 among medical frontliners in the National Cardiovascular Centre Harapan Kita of Indonesia. Our report aims to highlight asymptomatic and minimally symptomatic COVID-19 in immunocompetent adults, the effectiveness of PPE, and dangling risk of COVID-19 hitchhiking with cardiovascular diseases.

Case report

This is a case series of cardiology residents who developed COVID-19 in National Cardiovascular Centre Harapan Kita, Indonesia. Patients were screened based on close contacts with a positive case. Close contact was defined as exposure to a positive case within two meters for more than 30 minutes. A confirmed case was defined by a positive result on the standardized RT-PCR assay of a nasopharyngeal swab specimen. Cases with a positive rapid test without RT-PCR or negative RT-PCR result were excluded. Data were retrieved using a surveillance form and direct interview for additional information. Laboratory and radiographic findings were retrieved from the electronic medical record. This study was approved by the National Cardiovascular Centre Harapan Kita ethical review board. All participants had given their consent regarding their inclusion in the study.

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Table 1 Clinical, Laboratory, and Radiographic Findings.

Characteristics	Patients (n = 12)
Mean age (range) – year	29.9±1.88 (28-34)
Sex – no./total	
Male	6/12
Female	6/12
Care provider – no./total	
Self-care	12/12
Hospital	0/12
Comorbidities – no./total	
Hypertension	0/12
Diabetes mellitus	0/12
Asthma	5/12
Chronic obstructive pulmonary disease	0/12
Smoker	0/12
Symptoms – no./total	
Fever	2/12
Dry cough	3/12
Sputum production	0/12
Sore throat	2/12
Nasal congestion	2/12
Rhinorrhoea	1/12
Hyposmia	1/12
Hypogeusia	1/12
Headache	0/12
Conjunctival injection	0/12
Angina	0/12
Dyspnoea	1/12
Diarrhoea	1/12
Cutaneous manifestation	1/12
Fatigue	1/12
Asymptomatic – no./total	7/12
Mean temperature (range) – Celsius	36.6±0.95 (35.5-38.7)
Temperature > 37.5° C – no./total	2/12
Temperature > 38.0° C – no./total	1/12
Travel to endemic countries within previous month – no./total	0/12
Confirmed positive contact – no./total	12/12
Median onset of first symptom (range) – day	7 (5-24)
Standardized personal protective equipment – no./total	12/12
Full body wash before going home – no./total	12/12

Laboratory values	
Median leucocyte (range) – per mm ³	6350 (3870-8800)
Median thrombocyte (range) – per mm ³	251000 (163000-321000)
Median neutrophyl (range) – %	59.4 (52.2-88)
Median lymphocyte (range) – %	28.4 (6.6-39.5)
Median neutrophyl to lymphocyte ratio (range)	2.09 (1.32-13.3)
Median CRP (range) – mg/L	2.5 (0.3-46)
Radiographic examinations – no./total	
Chest x-ray	8/12
Pulmonary CT	1/12
Radiographic findings – no./total	
Infiltrate on chest x-ray	0/8
Pulmonary nodule on chest x-ray	0/8
Pleural effusion on chest x-ray	0/8
Ground glass appearance on pulmonary CT	0/1
Median communicable period (range) – days	16 (13-44)

Table 2 Clinical and Laboratory Findings of Each Patient.

	Patients											
	1	2	3	4	5	6	7	8	9	10	11	12
Comorbidities	-	-	Asthma	-	-	Asthma	-	-	-	Asthma	Asthma	Asthma
Symptoms	-	-	Sore throat	-	-	Dry cough	Fever (38.7° C), dry cough, sore throat, nasal congestion, hyposmia, hypogeusia, cutaneous exanthema	Fever (37.7° C)	-	Dry cough, nasal congestion, rhinorrhoea, dyspnoea, diarrhoea, fatigue	-	-
Leucocyte – per mm ³	7270	6020	4100	NA	6680	NA	8800	6540	3870	8290	4470	NA
Thrombocyte – per mm ³	319000	226000	175000	NA	306000	NA	163000	371000	253000	321000	249000	NA
Neutrophyl – %	60.2	55.7	55.9	NA	58.7	NA	88	70.3	52.2	74.8	68.2	NA
Lymphocyte – %	28.1	30.6	31.7	NA	28.7	NA	6.6	22	39.5	18.2	23.3	NA
Neutrophyl to lymphocyte ratio	2.14	1.82	1.76	NA	2.04	NA	13.3	3.19	1.32	4.11	2.93	NA
CRP – mg/L	3	1	19	NA	2	NA	46	2	0.3	2	4	NA

Not applicable.

Data were summarized using descriptive statistics. Numeric data were presented as means and standard deviations or median and minimum-maximum value as appropriate. Categorical data were presented as counts. The analysis was performed using IBM SPSS Statistics 22 software.

Clinical, laboratory and radiographic findings from this study were summarized in table 1. Twelve cases of COVID-19 were enrolled in this study. The mean age was 29.5 ± 1.38 . Six cases were males, and all cases were of Asian origin. There was no history of travel to endemic countries. The suspected source of transmission for each patient was illustrated in figure 1. The median time from initial contact to the first symptom was seven days. Asthma was the only comorbid found in this study. There was no hospitalization in this study. Leukopenia was observed in one patient. Increased C-reactive protein (CRP) value was observed in two patients. Lymphocytopenia was uncommon with median lymphocyte count of 28.1%. The median neutrophil-to-lymphocyte ratio (NLR) was 2.14. Chest radiograph was recorded in eight cases, and some are shown in figure 2. No lung infiltrates, pleural effusions, lung nodules, or ground glass appearances were seen. Experienced radiologists made radiologic evaluations.

Seven cases were asymptomatic, and five cases were minimally symptomatic. Fever was found in two cases with the highest temperature reported at 38.7°C . Other symptoms were dry cough, nasal congestion, rhinorrhoea, sore throat, diarrhoea, and fatigue. One case reported uncommon symptoms such as temporary hyposmia and hypogeusia with cutaneous exanthema and exfoliation. One case reported dyspnoea, but the symptom subsided with anti-asthmatic medication. None of the 12 patients developed signs of severe pneumonia. Clinical and laboratory findings for each patient were shown in table 2.

All cases had utilized PPE according to the hospital's policy. Standard PPE in the outpatient clinic was a head cap, surgical mask, face shield, regular scrub, disposable plastic apron, and gloves. Standard PPE in the isolation ward was a head cap, surgical mask on top of N95 mask, face shield, regular scrub, disposable coverall, double-layered gloves, a pair of latex boots, and shoe cover. There was no history of aerosol-generating procedure performed by all cases. The hospital also reinforced its personnel to take a bath before leaving the hospital.

By the time of data censoring all patients except for one converted from positive RT-PCR to negative RT-PCR. Median communicable period (interval from the first day of positive RT-PCR test to the first day of continuous negative RT-PCR test) was 16 days. One patient had an episode of re-infection. The re-infection lasted for seven days. Recoveries were excellent in all cases with no lingering symptom. There was no mortality in this study.

Discussion

In this case series, we describe 12 cases of COVID-19 infection among cardiology residents in National Cardiovascular Centre Harapan Kita. All patients are healthy adults in late twenties or early-thirties without previously known chronic disease other than controlled asthma in five cases. All cases are free from traditional cardiovascular risk factors. We observe a similar host response to COVID-19 infection with reports from other countries. Only two cases showed fever $> 37.5^\circ\text{C}$ while the rest was fever-free. Most patients in our study are either asymptomatic or mildly symptomatic.

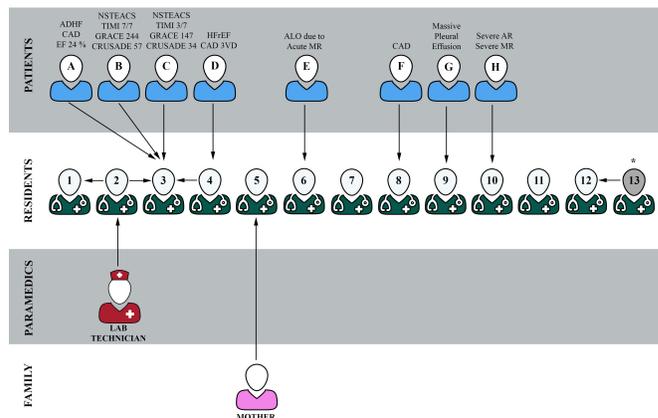


Figure 1: Suspected transmission diagram *: excluded due to unavailable data. ADHF: acute decompensated heart failure. ALO: acute lung oedema. AR: aortic regurgitation. CAD 3VD: coronary artery disease three-vessel disease. EF: ejection fraction. HFrEF: heart failure with reduced ejection fraction. MR: mitral regurgitation. NSTEMACS: non-ST elevation acute coronary syndrome.

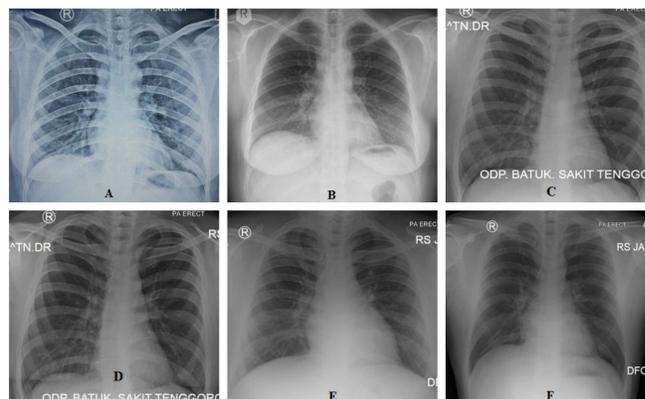


Figure 2: Chest x-ray from four patients. A: Initial chest x-ray from patient 3. B: Follow-up chest x-ray from patient 3 taken seven days later. C: Initial chest x-ray from patient 7. D: Follow-up chest x-ray from patient 7 taken 13 days later. E: Chest x-ray from patient 5. F: Chest x-ray from patient 1.

Leukopenia and lymphopenia were uncommon. Asymptomatic presentation of COVID-19 has been reported before [3]. It is possible to estimate the asymptomatic ratio of COVID-19 using binomial distribution and Bayesian theorem. This estimation is important because these asymptomatic patients cannot be recognized without the RT-PCR test, and they may potentially become silent spreaders [8]. Health care workers may unknowingly carry the risk of cross-infection, either to patients or other personnel in close proximities. The authority reports in China estimated that four-fifths of cases are alarmingly asymptomatic [9]. The significance of this finding is the necessity of massive RT-PCR screening in an otherwise asymptomatic population with close contact to identify silent spreader and prevent a potential outbreak. Social distancing with personal protection should be continued.

A dry cough is the most common finding in our study. It is understandable that in immunocompetent adults without comorbid or risk factor the infection expressed mild symptoms only. On the other hand, the senile population are associated

with higher mortality and morbidity due to immunosenescence [10, 11]. Senile naturally have a higher prevalence of comorbidity, especially cardiovascular diseases, and it has been associated with increased risk of death [11]. Our result suggests that fever may not be a reliable symptom to determine COVID-19 infection. Diagnostic algorithms and screening policies in public places that utilize fever as one of the criteria may delay the diagnosis and therefore, should be reviewed carefully.

There is a concern regarding PPE availability and distribution in Indonesia [7]. Due to global demand and disruption of supply chains, many of which are reliant on China, PPE supplies will remain to be uncertain [12]. Hoarders were buying N95 and surgical masks before the wake of COVID-19 in Indonesia to maximize profit. Nowadays the price is increased by almost tenfold of its normal value. Many clinicians express their fear that the frontliners do not have adequate protection due to shortage or inappropriate equipment [7]. The rate of physician death due to COVID-19 in Indonesia is 2.86% among total case fatality rate [13].

Most cases were transmitted during patient-doctor interaction. This may be caused by improper PPE donning or doffing. Doffing is very important because the sequences are being performed after direct contact with patients, thus carrying a high risk of self-contamination. A study reported a 90% error rate during doffing among healthcare workers in a viral respiratory infection setting concerning the sequence and technique [14]. In our hospital, we do not have many occurrences where health care personnel must wear level III protection. Hence the unfamiliarity with PPE donning and doffing. Another possible explanation is the PPE size. The N95 mask is not always fit on every person due to differences in facial feature such as nasal bridge and chin size. The leaky protective mask may potentially cause droplet or airborne transmission among frontliners.

Recent ESC guidance regarding diagnosis and management of cardiovascular disease during COVID-19 pandemic emphasizes population with cardiovascular risk factors or with established cardiovascular diseases are especially vulnerable with increased morbidity and mortality [11]. Inflammation due to viral infection is also capable of initiating coronary plaque destabilization (through tachycardia, hypoxia, increased wall stress, and released proinflammatory cytokines) and myocarditis [15]. Although our centre is not a designated COVID-19 referral hospital, due to their symptomatic similarities, sometimes COVID-19 patients are frequently overlooked and ended up in a non-isolated ward. These incidents should be prevented because of the risk of nosocomial transmission to other patients and attending health care personnel. Our study has several limitations. First, some cases had an incomplete laboratory and radiographic findings. To provide objective data, we did not approach patients to gather additional blood sample or radiologic examination. Second, only one patient has pulmonary CT scan result. Finally, our sample size is small and limited to a single centre only.

Conclusion

In healthy immunocompetent adults asymptomatic or minimally symptomatic COVID-19 infection is a common finding. Health care workers with silent infection may carry the risk of nosocomial transmission toward other workers or patients in care. Proper PPE donning and doffing technique must be practised at all time to prevent self-contamination.

Ethics approval and informed consent

This study has been approved by the National Cardiovascular Centre Harapan Kita Institutional Review Board.

Consent for publication

All patients have given their informed consent regarding the publication of this case series.

Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

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