The coincidence of dengue and Covid-19 in pandemic: Report of cases

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Abstract. Viral-based disease is very closely related to the climate change. For years, dengue infection was reported to be related to rainy season. Any climate change supposedly induces the change on the pattern of dengue infection. Since March 2020, the Covid-19 is started to report in Indonesia. The toll was relatively low in the beginning but gradually increased in the following months. In the same period of rainy season, as it is annually reported, the dengue fever is also increasing. The possible coincidence of covid-19 and dengue infection is therefore an interesting issue. We review 19 cases of which the Dengue fever serological test as well as Covid RT-PCR test were simultaneously performed based on the symptoms and signs found on the patient. Of those cases, coincidence was found on 4 cases. Even relatively low, the 4 cases were significant issue for public health management and the possible correlation with climate change. The emerging covid infection interfered with the dengue case infection along with the climate change. Those issues should be taken into consideration seriously for the health policies.

1. Introduction
Viral-based disease is very closely related to the climate change. For years, dengue infection was reported to be related to rainy season. Any climate change supposedly induces the change on the pattern of dengue infection. We have faced up and down in Indonesian cases of dengue infection during years [1]. On the other hand, coronavirus disease 2019 (COVID-19) is a respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has now spread to most countries around the world, resulting in a global pandemic [1]. SARS-CoV-2 is primarily transmitted from person-to-person through droplets while coughing and sneezing, from symptomatic and pre-symptomatic patients and probably from asymptomatic individuals as well [2]. Although there is yet no specific medication for treating COVID-19, multiple medicines are being assessed in clinical trials [3].

The first case of Covid-19 was reported on 2 March 2020. It was then transmitted and widespread to the whole country. Today, the number has reached more than 1.6 million confirmed cases in Indonesia. At the same time, dengue virus infection is an endemic disease mostly during the rainy season. It is estimated 77.96 cases/100,000 person-years in 2016. It has been a challenging health problem for years before COVID-19 was started to report. The pandemic is still ongoing in Asian countries in which dengue, caused by dengue virus (DENV), has been endemic for decades. Some countries in the region are facing dengue outbreaks amid the COVID-19 pandemic creating a double burden on resources and health systems [4].
There are similar symptoms and laboratory findings with both dengue fever and COVID-19, paving way to dangerous possibilities such as incorrect or delayed initial treatment. This is especially worrisome in the context of the pandemic, where COVID-19 positive patients must be promptly identified, isolated and contact-traced, and eluded diagnosis might endanger communities and healthcare workers. In addition, with similar clinical symptoms for both diseases, this creates a critical problem of misdiagnosis and the possibility of double infection occurring within the same individual at the same time.

2. Methods
The diagnosis of covid-19 was made based on the Indonesian Ministry of Health Standard [5]. While the diagnosis of DHF was made based on WHO criteria that have been ratified by the Indonesian Ministry of Health [6]. Some items such as fever, low platelet count, coagulation factor imbalance, have been in common both of the diseases. During presentation to the hospital, some patients showed chronology and physical examination in common between Covid-19 and DHF patients. On several occasions, the patient showed similar symptoms and signs of both conditions. Among those patients, the attending doctor will order anti-dengue IgM/IgG antibody test for a possibility of missed case and or history of DHF. In addition, RT-PCR Covid-19 was applied for suspicion of covid-19. The study was conducted at Sebelas Maret University in 2020. The cases with laboratory showed coincidence of covid-19 case, as well as DHF, were being the subjects of analyses. The analyses will focus on the aspect of laboratory results with several related signs and clinical points.

3. Results
During 2020, there were 802 covid-19 suspect and 737 confirmed cases of covid-19. During the same period, there were 303 dengue hemorrhagic patients (DHF). In the previous 2019, the number of DHF cases was 369. The decrease of DHF number was indicated in relation with the outbreak that there were overall decrease of non-covid-19 visit to the hospital.

Among those, there were 33 cases when the symptom, sign and history indicate the possibility of covid as well as DHF. On 19 of 33 cases, SARS CoV 2 RT-PCR was conducted. In the remaining cases, rapid anti-SARS-CoV-2 antibody were only conducted with nonreactive results and no RT-PCR were conducted later. Among 19 cases, there 4 cases with co-infection Covid-19 and DHF. The analyses are as follows on the next section.

4. Case analyses and discussion

4.1. 1# Case
Man, 27 years old, presented with a history of fever during the last 10 days, up and down, accompanied by cough and shortness of breath. The patient also reported myalgia and anorexia. The vital sign showed respiratory rate of 24/minute and SpO2 as 92%. The laboratory results showed NLR of 5,10 and ALC 770/microliter. Platelet count was 111.000/microliter. D-dimer was 799 ng/mL, albumin 3,5 g/L. Serology tests were reactive for IgM and IgG anti-dengue. The swab for SARS CoV 2 RT-PCR was collected and reported a day later to be positive and confirmed as covid-19 case. The platelet count was getting higher day by day and reached normal value on the 4th day of care as 202.000/microliter. It was parallel with improvement of covid-19 clinical sign as well as laboratory results. NLR was lowering and ALC was increasing to be 1360 on the 10th day of care. The evaluation test of SARS CoV 2 RT-PCR showed positive result on the 7th day but becoming negative on 10th day. The patient was then discharged with stable and well condition. The duration of case was suited to Indonesian Standard of Care for covid-19 case [5].

This #1 case showed a rather normal natural history of dengue virus infection with pulse fever and low platelet count that was becoming normal count on the 4th day of care. While the covid-19 natural history also showed a normal pattern with improvement of NLR dan ACL on the 10th day together
with SARS CoV 2 RT-PCR was also becoming negative. The young age, and no serious comorbidity findings, were indicated to be the supporting factor of favor improvement.

4.2. 2# case

Man, 23 years old, presented with report of 5 days fever, with temporary lower body temperature during 2 last days before presentation. It was 28.7 cents degree. The patient also reported myalgia and sore throat. No cough and shortness of breath were reported. The platelet count was 116,000/microliter. Along with symptoms and signs, it was suspect of dengue virus infection. NLR was 3.33 and ALC was 760/microliter indicating risk of a covid-19 case. Serology of dengue virus infection showed reactivity of IgM and IgG. While the rapid anti-SARS-CoV-2 antibody test was nonreactive. The results of SARS CoV 2 RT-PCR reported a day later were positive. The working diagnose was dengue virus infection with Covid-19.

The platelet count becomes lower the next day, then gradually increased during the next days and becoming normal count on the 6th day of care. It was also reported pneumonia with K pneumonia and P aeruginosa finding on the culture. That pneumonia was becoming the main problem that lengthen the length of stay. The clinical sign then showed improvement. The evaluation of SARS-CoV-2 RT-PCR showed positive results on the 7th day of care before becoming negative on the 14th day of care. This #2 case also showed a rather normal natural history of dengue virus infection with pulse fever and low platelet count. The decreasing platelet count on the 2nd day showed an acute period of dengue viral infection. After then, the platelet count was gradually increased to becoming normal on the 6th day of care.

While the covid-19 natural history also showed a rather normal pattern even more severe than the #1 case. The finding of bacteria causing pneumonia as secondary infection on the covid-19 lengthen the timeline for recovery. The covid-19 gradually showed improvement. The SARS CoV 2 RT-PCR took 14 days to become negative. The patient as young as the #1 case. But serious findings on pneumonia were indicated to be the factor for more severe and longer duration of treatment.

In those #1 case and #2 case, there were no significant indications for dengue viral infection render the amelioration of covid-19 as well as vice versa.

4.3. 3# Case

Man, 66 years old with history of TB (second month of 6 months ongoing course of therapy). The patient presented with productive cough, shortness of breath and sore throat. Fever was denied. The patient reported traveling to the area with widespread of covid-19 7 days before presentation. The rapid anti-SARS-CoV-2 antibody test had been conducted before presentation with reactivity results.

Laboratory results showed low platelet count was 87,000/microliter, D-dimer was 1.473, HbA1c was 9.3% and reactive HBsAg test. Blood glucose was 294 g/dL. The blood gas analysis showed metabolic alkalosis with respiratory compensation. The following results of the laboratory during days of care showed also more comorbidity with type II Diabetes mellitus and dyslipidemia. On the 5th day of care, dengue virus infection was indicated, and IgG reactivity was found. NLR was 0.18 and ALC 1.680 of which were not indicative for Covid-19. The SARS CoV-2 RT-PCR result reported a day later was positive. It was suspected of secondary dengue virus infection on the confirmed case of covid-19.

The patient was being in the care for 18 days. The platelet count was decreasing before slowly getting increased and becoming on the 14th day of care. It was longer than the normal natural history of dengue infection period. The co-infection and comorbidity was indicate to lengthen the recovery of platelet count than isolated dengue virus infection period. Age was also a factor to consider. The SARS CoV 2 RT-PCR evaluation test showed positive results 10th day of care, followed by negative results on the 17th day of care. The patient was discharged and followed by regular visit to outpatient clinic for comorbidity care. Compared to the previous #1 and #2 cases, the #3 case was older and presented with more severe comorbidity. The duration of covid-19, as well as DHF, was getting longer.
and slower. The case should be very warned for risk of reinfection with covid-19.

4.4. 4# case
Woman, 81 years old, presented with unconsciousness, shortness of breath, with no fever and cough. A history of diabetes Mellitus and hypertension were not found. The laboratory data, it showed hypoglycemia, decrease in liver function test, acute kidney injury and low platelet count (15,000/microliter). The serology test for DHF showed IgG without IgM reactivity. Neutrophil lymphocyte ratio (NLR) was 49.35 and Absolute Lymphocyte count (ALC) 340. These two were strong indicators for covid-19 risk. Blood gas analysis showed metabolic acidosis with not perfect respiratory compensation. Hypoxemia was also indicated. The patient was worsening soon and finally was called as a death case 14 hours in the intensive care unit (ICU). So far, the status was a probable covid-19 and secondary dengue virus infection. The probable status was made based on strong indication in the sign, clinical findings and laboratory results were very indicative. Before being a death case, the swab for SARS Cov 2 RT-PCR was collected. The information came a day later with negative results. Based on the diagnostic standard of the Indonesian Ministry of Health (MoH), one negative result does not rule out the covid-19 diagnosis. It has to be two swabs to collect with 24 hours interval for the final laboratory diagnosis of SARS CoV 2 RT-PCR. Since it was not possible to collect the second swab, the final status is probable. The #4 case showed more complex infection. The severe condition at presentation, decrease the opportunity for more robust care and detailed laboratory tests. It was also no complete data were collected for very short duration of care. Very old age might induce frailty that renders the improvement from infection.

4.5. #5. Overall discussion
The study did not detect cross-reactivity reported by Tiwari et al (2020) [7]. The detection of anti-dengue antibodies was not dependent on the Anti-SARS-CoV-2 antibody. The study did not conduct re-testing of Anti Dengue antibody to detect any change. But considering the clinical findings, on the #1 and #2 case were clear that those were co-infection and was not merely a serological overlap [8], [9]. While on the #3 and #4 case, the probability was not impossible since they were suggested as secondary infections.

It was reported also from a survey in Bangladesh, collecting responses from 1590 different social groups (healthcare professionals, academicians, students, NGOs, and government officers) suggested that climate change would induce significant impact on the infectious disease transmission and pattern. This should be embraced with risk assessment and communication, lack of sectoral coordination for better readiness [10].

5. Conclusions
The co-infection of dengue virus infection and covid-19 were a small number but significant issue. The natural history during days of care was varied inferred by the age of patients as well as the comorbidity. In the eye of public health, those two infections might induce double burden. These issues should be embraced gently and carefully since the combination and interrelated between the factors of patient as well as clinical and environmental. As the climate might induces change in the temporal pattern of viral infection, it is a challenging to elucidate more in the context of dengue and SARS CoV 2 viral coincidence infection. That is very important for an archipelago such as Indonesia.

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