Case report of a COVID-19 family cluster originating from a boarding school

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Since it was first identified in Wuhan City, Hubei Province, China in December 2019, SARS-CoV-2 has spread to 195 countries and infected more than 8 million people globally. Indonesia, an archipelago consisting of thousands of islands and 34 provinces, has the largest number of confirmed cases and mortality in Southeast Asia. A total of 464 districts/cities in Indonesia have been affected by COVID-19, of which 189 districts/cities are considered to be local transmission areas. Riau Province, located in Sumatra Island, consists of 12 districts/cities with a population of more than 6.8 million. This province has the 1st largest number of COVID-19 cases on Sumatra Island. Currently, more than 3000 children have been infected with case fatality rate <0.3% and recovery rate >90%. In May 2020, the public health office of Riau reported that just 34 children were confirmed to have COVID-19, with symptoms varying from asymptomatic to moderate with only a few family clusters identified. During the pandemic, contact tracing is the main approach to detect and isolate sources of infection in order to reduce viral transmission. This method has also been used to control transmission of other respiratory diseases such as tuberculosis (TB), MERS, and SARS. We report here on a familial cluster of COVID-19 in the Meranti Island Regency, which is located 145 km from the city of Pekanbaru (Riau Province). The island can only be reached in four hours by speed boat. [Paediatr Indones. 2021;61:53-60; DOI: 10.14238/pi61.1.2021.53-60].

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The Case

On April 16, 2020 the Malaysia Ministry of Health announced a new cluster of COVID-19 from students returning from a boarding school in Temboro, Magetan Regency, East Java, Indonesia, with 43 Malaysian students confirmed to have COVID-19 upon their return to Malaysia. Since that time, the Indonesian government has coordinated with COVID task forces in various provinces to trace students who returned to their respective homes. Several provinces reported confirmed COVID-19 cases from the Magetan cluster, including Aceh, West Sumatra, Riau, East Kalimantan, and East Nusa Tenggara. The case from the Magetan cluster in Riau Province was first discovered in the Indragiri Hilir District. A 19-year-old boy was successfully traced. His rapid
diagnostic test (RDT) for antibodies and reverse transcription-polymerase chain reaction (RT-PCR) swab for SARS-CoV-2 showed positive results. He returned to Riau from Magetan on April 12, 2020. Information about the number of other students from Magetan was obtained from him. Other students went to various regencies/cities in Riau, namely Indragiri Hilir, Bengkalis, Pelalawan, Siak Regency, Meranti Island, and Dumai City, using private vehicles and did not report to their local health departments.

In the Meranti Islands Regency, the District Health Office traced students originating from Magetan and conducted RDT, RT-PCR swabs, laboratory examinations, and chest computerized tomography (CT scans). As of May 10, 2020 there were 10 children aged 0-18 years who lived in Meranti Islands Regency suspected to have COVID-19, of whom 4 of them were boarding school students from Magetan and confirmed later of being infected with SARS-CoV-2. The exact data on the number of students from Magetan who returned to Meranti was unknown because they returned back to Meranti Islands independently without reporting to the local health office, so the data for 4 people were obtained from information from fellow students who knew each other.

On May 14, 2020, a 17-year-old male student (A1) tested positive by PCR swab after having been traced by the Meranti District Health Office. He complained only of pain when swallowing; he had no fever, cough, shortness of breath, or chest tightness. A rapid antibody test was positive, so the patient was isolated and contact tracing was performed. From contact tracing 6 people were found to have close contact with A1. His family, consisting 5 persons, including his father, mother, 3 children and also 1 close friend (Table 2). The mother (A2), brother (A3), sister (A4), and close friend (A5) also had RDT and RT-PCR positive results, even though none had symptoms (Figures 1 and 2). Despite living on the same roof as A1-A4, A6 showed negative RT-PCR results.

The five family members and one friend were interviewed. Previously, A2-A4 came to pick A1 up at the airport, then travel overland using private car from Sultan Syarif Qasyim Pekanbaru Airport to Meranti Island. It took approximately 1 hour drive from airport to Sungai Duku Harbor, 5-6 hours from Sungai Duku Harbor to Meranti Island using fast ferry, and another 3-4 hour drive from harbor to the patient’s home. During the trip, A1-A4 often open their mask. A5 did not live in the same house as A1, however, had close contacts with A1 almost every day within 14 days. From the 5 members of this family cluster, only A1 had a complaint of hoarseness, while others had no complaints.

A1-A5 were diagnosed positive with SARS-CoV-2, according to the Guidelines of COVID-19 Control and Prevention version 4 by Directorate General of COVID-19 Control and Prevention. Epidemiological, demographic, clinical, and laboratory testing data were obtained from patients’ medical records. nasopharyngeal swab specimens were maintained in viral-transport medium. The SARS-CoV-2 was confirmed by RT-PCR by using the protocol described previously.

According to Riau’s Task Force Protocol that current time, all COVID-19 confirmed patients must be isolated in the hospital regardless of the results. Thus, case A1-A5 were all hospitalized in a district

| Case | Age, years | Gender | Relation to index case | Symptoms | Date of positive RT-PCR | Number of days since potential exposure | Date of negative RT-PCR | Positive PCR duration |
|------|------------|--------|------------------------|----------|-------------------------|----------------------------------------|------------------------|----------------------|
| A1   | 17         | M      | Index case             | Sore throat | May 14, 2020            | Unknown                               | May 18, 2020            | 3 days               |
| A2   | 40         | F      | Mother                 | None      | May 15, 2020            | unknown                               | May 20, 2020            | 5 days               |
| A3   | 18         | M      | Brother                | None      | May 15, 2020            | unknown                               | May 20, 2020            | 5 days               |
| A4   | 11         | F      | Sister                 | None      | May 15, 2020            | unknown                               | May 31, 2020            | 17 days              |
| A5   | 17         | F      | Friend                 | None      | May 25, 2020            | unknown                               | June 1, 2020            | 8 days               |
| A6   | 39         | M      | Father                 | None      | Negative                | -                                     | -                      | -                   |
After the RT-PCR results of A1 showed positive (May 14, 2020), A1 was immediately admitted to the hospital and was treated for 10 days (from May 14, 2020 to May 24, 2020). A4 was treated in the hospital for 15 days (from May 14, 2020 to June 3, 2020), meanwhile A5 for 20 days (from May 24, 2020 to June 10, 2020).

The laboratory test results were within normal limits. All patients underwent chest CT-scan; a ground glass appearance was identified in only A4 and A5 (Figure 3 and Figure 4). None of the patients...
Figure 3. CT scan image of case A4

Figure 4. CT scan image of case A5
had leukopenia, thrombocytopenia, monocytosis, increased neutrophil-to-lymphocyte (NLR) ratio or decreased absolute-lymphocyte-count (ALC).

Follow up RT PCR was performed to the three subjects. A1 had negative results in swab-2 (May 18, 2020) and swab-3 (May 20, 2020). A4 had positive result in swab-2 (May 16, 2020), negative in swab-3 (May 24, 2020), went back positive on swab 4-5 (25 and May 27, 2020) and finally negative on swab-6 and -7 (May 31, 2020 and June 1, 2020, respectively). A5, showed positive swab-2 results (May 27, 2020) and negative on swab-3 and -4 (May 31, 2020 and June 1, 2020).

Discussion

Here we describe the spread of COVID-19 from a student living in congregate housing to his family and friend after returning home from school. The symptoms in the index case and his contacts varied from asymptomatic to mild. Previous studies suggest that children tend to have milder SARS-CoV-2 infections compared to adults.2-5 Approximately 20% of 171 PCR-confirmed cases showed to be asymptomatic in children and adolescents.6 Likewise, children with COVID-19 more commonly have normal laboratory results compared to adults.2,3,5-7 However, CT imaging varies among patients, from showing normal/no signs of pneumonia to ground glass opacities.2,3,5,8

Children, especially younger ones, tend to have various viral infections. The milder course of COVID in children might be due to their repeated viral exposure supports the immune system in responding COVID-19.2 The presence of simultaneous viruses in the mucosa of the lungs and airways, commonly found in children may limit the growth of SARS-CoV-2 by direct virus-to-virus interactions and competition. SARS-CoV-2 binds and enter the body through the angiotensin-converting-enzyme (ACE).2,9-10 It has been hypothesized that this enzyme may be less mature in children, thus, protecting children from more severe course of disease.8 A study described ACE2 gene expression to be higher in older children (10-17 year old) and adults (≥17 years old) compared to younger children (<10 year old). Another study found that ACE 2 protein expression is significantly higher in adults compared to infants and toddlers (<5 years old).10 Despite children’s tendency to have milder COVID-19 symptoms, it is important to make elderly caregivers aware of the risk of transmission from young children.2

Real-time RT-PCR is the standard diagnostic method for COVID-19. Although it is very specific, this method has lower sensitivity in mild symptoms patients (62.5% compared to 78.2%)11 and a long waiting time, generally requires a minimum of 2 days waiting time for results in some regions of Indonesia. This method may show false negative results (2-24% of cases).12 As in case A4, the 3rd swab showed negative results while the next two swabs showed positive. Researchers in John Hopkins University declared that false negative results occur in 1 from 5 RT-PCR samples. This may be caused by genetic diversity, sampling errors, sample types, and the viral load.13 The evolution of the virus creates a variation in viral sequences that may cause mismatches between target regions and primers. Sampling errors such as inadequate sample collection, incorrect sampling technique, inexperienced healthcare professional, improper sample handling.14 Sputum is found to be accurate followed by nasal swabs. However, the virus may travel down to the lower respiratory tract overtime which cause this sampling more suitable to be done in earlier course of disease.14 Maximum viral load is found 5 days after symptom onset, and the viral loads are similar to the asymptomatic patients.14 In this case, 1st and 2nd swabs have shown positive results, thus we believe the negative result on the 3rd swab may be caused by sampling errors. Chest radiographs and CT-scan may contribute to early detection of lung abnormalities and help rectify false negatives in RT-PCR results.15

All the children in this case study had negative RT-PCR results after 5-17 days. Although patient A4 experienced negative result on the 3rd swab, and results came back positive on 4th and 5th swab eventually she showed no symptoms. A previous study suggested that although patients appear to have a long period of positive PCR results, in treated patients, nasopharyngeal viral load of COVID-19 was cleared in only 3 to 6 days, and virus cannot be isolated after day 8, in spite of ongoing high viral loads of approximately 10^5 RNA copies/mL of sample.16 The prolonged positive results initially lead to long
hospitalization times. The viral load surrogate marker in PCR is the cycle threshold value (Ct value). Patients with Ct value of 34 or above are believed to no longer excrete infectious viral particles.\textsuperscript{16,17}

As there is no definitive treatment for COVID-19, non-pharmacological interventions such as self-isolation, voluntary home quarantine, social distancing, as well as closure of schools and universities remain important approaches in preventing disease spread.\textsuperscript{18} A 14-day minimum quarantine time has been recommended, however, a study showed that 1\% of the cases that have undergone 14 days of quarantine have the probability to still be positive.\textsuperscript{4,19} Chen et al.\textsuperscript{5} reported that the 4 family members of their case series were diagnosed with COVID-19 after undergoing a 14-day quarantine. Thus, they suggested a longer period of self-quarantine. Another study suggested a quarantine duration of 2 months.\textsuperscript{4} Since quarantine requires staying indoors for a long time, decreased human communication may affect personal mental health, such as anxiety-related behaviors, stress disorders, and environmental risks, such as exposure to smoke from cooking fires. Thus, prolonged quarantines may worsen other risks.\textsuperscript{20} In addition to quarantine, immediate examination of 3 family generations should be conducted, especially if they live together.\textsuperscript{4}

In the previous guideline, discharge criteria constitutes 2 negative consecutive results. In this case, case A1 and A5 both were hospitalized for 6 days and discharged after showing two negative results. Meanwhile A4 was hospitalized for 17 days and discharged after having two consecutive results. The current guideline, Guideline of COVID-19 Control and Prevention version 5, recommends that patients can be discharged from hospital or stop quarantine time 10 days after the onset of symptoms plus 3 days of symptoms free (fever or respiratory symptoms) and 10 days after positive result of SARS-CoV-2 PCR for asymptomatic patients, despite swab results.\textsuperscript{21} False positive results may occur due to sample contamination of samples and/or reagen, during sample processing.\textsuperscript{22} Other than that, RT-PCR examination can not differentiate live and dead virus, thus may cause false positive results.\textsuperscript{23}

In this case, A1 travelled from his boarding school in East Java to his hometown in Riau, suspected to have transmitted the virus to other family members and a friend. Students living in congregate housing at school are especially prone not only to viral transmission among students, but eventual transmission to their families after travel. As such, the government should develop regulations to reduce the risk of COVID-19 transmission in congregate housing, as well as viral after travelling.

This report has several limitations, such as not measuring viral load by cyclic threshold on RT-PCR. Some COVID-19 cases have positive PCR results for prolonged periods after symptom resolution. It is not clear whether this indicates viable virus. If so, before stopping isolation measures, it might be necessary to confirm that the patient has negative PCR result. Both the aforementioned and the recognition of subclinical infection could potentially decrease the probability of fully controlling the outbreaks due to both sorts of individuals could be important sources of infection. Secondly, more virologic data is needed. Virus culture was very costly, thus, not performed in those who remained positive by PCR examination. Thirdly, considering that A1-A4 live separately from A5, it couldn’t be determined whether A5 caught the virus from A1. Detailed sequence analysis was not available, which might help us to clarify the transmission chains within the families and friend.

As SARS-CoV-2 is a highly contagious virus, effective intervention measures should be adopted for the prevention of family transmission when boarding students return to their hometowns after residing in congregate housing. Children and adolescents tend to have milder symptoms compared to adults; however, they are potentially infectious. RT-PCR swab results may remain positive more than 14 days after symptoms appear, which can be caused by detection of RNA fragments. The Ct value from RT-PCR may help to determine if an individual is still infectious, so that the next course of action can be recommended.

Since December 2019, COVID-19 has spread globally including Indonesia. Reports stated that pediatric cases are mostly owing to family cluster and close contacts history. As in this case spread through school and home. The disease manifest in children mostly as asymptomatic or mild disease, which are recommended to do self- or hospital isolation. Previous guidelines suggest to have two consecutive negative RT-PCR to discharge a patient from isolation. On the latest guideline, RT PCR evaluation is not
required to be performed in asymptomatic and mild symptom patients, instead, these patient allowed to be discharged after fulfilling minimum quarantine time. Ten days isolation after onset of symptoms plus 3 days of symptoms free and 10 days isolation since positive results in asymptomatic patients Studies has shown false positive results may occur which may cause prolonged hospitalization that gives loss in the matter of cost and patient's mentality. Other than that, persistent positive results does not necessarily show its infectivity. The Ct value examination may help to picture the infectivity of the disease after showing positive results.

Conflict of Interest

None declared.

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