Literature Review

The difference in severity and management between children and adult’s cases of COVID-19

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ABSTRACT

COVID-19 (Coronavirus Disease 2019) has been started in Wuhan, China, and spread worldwide and resulting in many cases of death. COVID-19 attacks the respiratory tract acutely and infected both children and adults. The number of cases in children is less than in adults. By seeing from the clinical aspect, the COVID-19 case in children is milder. There are differences in immunology responses in children and adults where children have higher immunology response of COVID-19 than adults. Meanwhile, if the immunology response is slow in adults, it may cause them infected by COVID-19 with severe symptoms. There are some relations between immunization with immunology response to SARS-CoV-2 where children who already have BCG vaccination has lower infection rates of acute respiratory tract case. This study aims to know the difference between COVID-19 cases that infected adults and children seen in various aspects.
INTRODUCTION

The COVID-19 (Coronavirus Disease 2019) pandemic situation consists of a collection of severe acute respiratory diseases that threaten human health in the world (Rothen and Byrareddy 2020). Covid-19 infection in children under 15 years old is less than that of the adult, and the symptoms are milder. The epidemiological evidence stated that the number of deaths in pediatric cases is also lower than the adult, and there is a biological difference between children and adults (Sighn et al., 2017).

The case number COVID-19 in the world at the date of 27 November 2020 has reached 60,264,241 cases with many deaths of 1,420,306 patients (World Health Organization (WHO), 2020). The Indonesian Ministry of Health reported 522,581 cases of COVID-19 on 27 November 2020 (KEMENKES, 2020). COVID-19 case in children is fewer than in adults. 72,314 recorded positive COVID-19 in China, with 2% of the patients under 19 years old. Italy is one of the countries that experienced the pandemic’s impact, with 1,2% of all children. Italy also has higher cases than China (7,2% vs 2,3%), but there is no mortality rate for children (Liguro et al., 2020). It is recorded that 535 out of 113,368 COVID-19 cases are infected children under 18 years old in Spain (Melgosa et al., 2020). Not only in Italy, China, and Spain but also in children and Africa and America. From March until April 2020, there are 5,2% cases of children infected by SARS-CoV-2 out of 474 recorded cases (Bandi et al., 2020).

The number of deaths caused by COVID-19 in China is 2,3% (1,023 death cases out of 44,672 confirmed cases). There were no cases of death in 9 years old group and younger, but the case was found in 70 until 79 years old group, which has a death rate of 8,0%, and the case in 80 years old group or older has a death rate of 14,8% (Wu dan McGoogan, 2020).

Total number positive COVID-19 cases in Indonesia up until November 2020 reach 522,581. Active cases 68,604, recovered cases 437,456 and number of death cases 16,521.

LITERATURE REVIEW

Virology of SARS-CoV-2

The SARS-CoV-2 is an RNA (ribonucleic acid) virus with a small 120-160 nm size. 6 types of coronavirus can infect humans; they are alphacoronavirus 229E, alphacoronavirus NL63, betacoronavirus OC43, betacoronavirus HKU1, Severe Acute Respiratory Illness Coronavirus (SARS-CoV), and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (Brooks et al., 2013).

The SARS-CoV-2 is included as one of the beta coronavirus genus, and many reports of phylogenetic stated that SARS-CoV-2 has the same subgenus with SARS virus component, which included as Sarbecovirus genus (Zhu et al., 2020). The SARS-CoV-2 also has similarity with SARS-CoV-2 gained from a bat and isolated, so there was a suspicion that SARS-CoV-2 is from mutated bats and infected humans (Zhou et al., 2020).

The computer test stated that the SARS-CoV-2 virus has a 3 dimension structure, including protein spike receptor-binding, and has a very strong affinity for angiotensin-converting-enzyme 2 (ACE2) (Zhang et al., 2020).

The SARS-CoV-2 has S-protein or spike protein
The case of children in China until N reached 2143 positive cases. The asymptomatic case in children (94), mild case (1091), moderate case (831), severe case (112), and critical case (13) (Dong et al. 2020). The severe case found in China and Italy reached 19% and 26% for adults older than 60 years old (Istituto Superiore di Sanità 2020a; Wu and McGoogan 2020). The death rate of children in Indonesia until mid-July 2020 is 2,06% for 0-5 years old and 0,50% for 6-17 years old (Setiabudi 2020).

From the report mentioned above, the number of adult’s cases are higher than pediatric cases.

Pathogenesis and pathophysiology of coronavirus in pediatric and adults

The SARS-CoV-2 passes the respiratory tract and is attached to Angiotsinsin-Converting Enzym-2 (ACE-2) using the spike protein structure of SARS-CoV-2. The ACE-2 receptor can also recognize SARS-CoV (Dhochak et al., 2020; Hoffmann et al., 2020). The ACE-2 can be found in many organs, including oral mucosa, nasal, nasopharynx, lung, stomach, small intestine, large intestine, skin, thymus, bone marrow, spleen, liver, kidney, brain, pulmonary alveolar epithelial cells, small

Table 1. SARS-CoV-2 confirmed patient cases in children and adults.

| Characteristics | Children | Children | Children | Adults | Adults | Adults |
|-----------------|----------|----------|----------|--------|--------|--------|
| Number of patients | 2572 | 171 | 105.040 | 113.985 | 1099 | 417.541 |
| Age | <18 years old | <16 years old | <18 years old | 18-64 years old | >15 years old | >18 years old |
| Region | United States | China | Indonesia | United States | China | Indonesia |

Source: CDC COVID-19 Response Team, 2020; IDAI, 2020; Lu et al., 2020; Wu & McGoogan, 2020; SATGAS COVID-19, 2020
intestinal enterocyte cells, endothelial cells
venous arteries, and smooth muscle cells
(PDPI, 2020).

The SARS-CoV-2 enters the cell facilitated
by proteolytic breakdown ACE-2 by
transmembrane serine protease-2 (Dhochak
et al., 2020; Hoffmann et al., 2020). Inside
the cell, the RNA genome virus is released
to the cytoplasm and then translated into two
polyprotein and structural proteins. After
being translated, the virus genome begins to
multiply itself. The new glycoproteins which
are formed on the virus’s surface, started to
go inside the endoplasm reticulum membrane
and the virus started to grow and forms
nucleocapsid. In the last stage, the vesicles
that already contain the virus start to combine
with plasm membranes that have the purpose
of releasing the new virus components (Susilo
et al., 2020; de Wit et al., 2016).

Patients infected by SARS-CoV-2
experiencing a decrease of ACE-2 regulation
that results in increased vascular permeability
and inflammation. The ACE-2 activity in
children is very high to give protection
from SARS-CoV-2 infection manifestation
and reduce the severity level case (Cristiani
et al. 2020; Dhochak et al. 2020; de Wit et
al. 2016). The result from recent studies, it is
still hard to predict that ACE-2 activity in the
lungs is more important than SARS-CoV-2
because the infection of SARS-CoV-2 is more
severe clinically in infants rather than the older
children (Dhochak et al. 2020).

The difference between adults and children
case is related to living habits and host factors.
Children are tended to play at home and are
taken care of by the parents, so they have a
lower chance of infected by the pathogens.
Meanwhile, adults have a responsibility to
work, etc., which have a higher chance of
infected by the pathogens. Children are also
less sensitive to SARS-CoV-2 because of the
maturity, function, and number of the ACE-
2. Besides the ACE-2 factor, children often
experience respiratory tract infections that
might have a higher antibody level to the virus,
and the immune of children still develops and
might recognize the pathogens differently than
adults (Dong et al. 2020).

**Figure 1.** The difference of ACE-2 expression in pediatric and adults infected with SARS-CoV-2
(Cristiani et al. 2020; Dhochak et al. 2020; de Wit et al. 2016).
The clinical symptoms of pediatric and adult cases

The clinical symptoms of children infected by SARS-CoV-2 now are milder than the adult infected by SARS-CoV-2. More studies in pediatric SARS COV-2 was conducted; it is now clear that children of any age can be infected. But the case is more difficult to detect since they are likely to be asymptomatic and the possibility to get tested is small (Dong et al., 2020; Lu et al. 2020; Sighn et al. 2017).

The main SARS-CoV-2 symptoms are fever and cough. Some patients experience dyspnea, vomit, diarrhea, myalgia, and fatigue. The fever symptoms in children are only 51.6%, cough 47.3%, and sore throat 17.9%. A few children are infected with SARS-CoV-2 who experienced dyspnea and decreased oxygen levels (7.7% and 9.7%) (Liguoro et al., 2020; Lu et al., 2020; Sun et al., 2020). Other symptoms outside the respiratory are found in children infected by SARS-CoV-2, which is diarrhea (9.7%), vomit (7.2%), and fatigue (10.6%) (Liguoro et al., 2020).

The most common symptoms in adult infected by SARS-CoV-2 is fever (98%), cough (76%), dyspnea (55%), and muscle ache or fatigue (44%). In another study, the symptoms in an adult patient of 70 years old or older are also found shortness of breathing (76%), fever (52%), and cough (48%). The adult case with covid-19, a 86% had comorbid diseases such as chronic kidney disease (48%), congestive kidney failure (43%), chronic obstructive pulmonary disease (33%), and diabetes (33%) (Shahid et al., 2020)

Total calculation of a (n=1016), Total calculation of b (n=2,572), Total calculation of c (n=113,985), and calculation of d (n=41).

The COVID-19 classification in pediatric

COVID-19 cases classification consists of asymptomatic cases, mild cases, moderate cases, severe cases, and critical cases.

A. Asymptomatic case : test results were positive with no clinical signs and symptoms

B. Mild case : Has symptoms of an upper respiratory tract infection such as fever, fatigue, myalgia, cough, sore throat, cold, and sneezing. In some cases, it may have no symptoms of an upper respiratory tract infection and is only accompanied by gastrointestinal symptoms such as nausea, vomiting, abdominal pain, diarrhea, or other non-respiratory symptoms.

C. Moderate case : sign and clinical symptoms of pneumonia. Fever, cough, tachypnea, can be accompanied by rhonchi or wheezing in lung auscultation without respiratory distress and hypoxemia.

Table 2. Clinical symptoms of SARS-CoV-2 in the case of pediatric and adults

|                | Pediatric | Adults | Pediatric | Adults |
|----------------|-----------|--------|-----------|--------|
| Fever          | 163 (56)  | 7.794 (71) | 503 (51,6) | 40 (98) |
| Cough          | 158 (54)  | 8775 (80) | 461 (47,3) | 37 (76) |
| Sore throat    | 71 (24)   | 3.795 (35) | 174 (17,9) |        |
| Dyspnea        | 39 (13)   | 4674 (43) | 22 (55)   |        |
| Diarrhea       | 37 (13)   | 3.353 (31) | 94 (9,7)   |        |
| Vomiting       | 31 (11)   | 1.746 (16) | 70 (7,2)   |        |
| Headache       | 81 (28)   | 6.335 (58) | 3 (8)      |        |
| Myalgia / Limp | 66 (23)   | 6.713 (6,9) | 103 (10,6) | 18 (44) |

Source: CDC COVID-19 Response Team, 2020; Huang et al., 2020; Liguoro et al., 2020
D. Severe case: Has clinical symptoms of severe pneumonia such as nostril breathing, cyanosis, subcostal retraction, desaturation (oxygen saturation <92%). In some cases, it may have common dangerous clinical symptoms such as seizures, decreased consciousness, profuse vomiting, and unable to drink, with or without respiratory symptoms.

E. Critical case: Patients rapidly experience Acute Respiratory Syndrome (ARDS) or respiratory failure, or experienced shock, encephalopathy, myocardial damage, coagulopathy, acute renal failure, and multiple organ dysfunctions or other manifestations of sepsis.

F. Multisystem inflammatory syndrome: children and adolescent aged 0-19 years old with 3 days fever, accompanied by minimum 2 of the following:
   a. Rash or bilateral non-purulent conjunctivitis or sign of oral, hand, or foot mucocutaneous inflammation
   b. Hypotension or shock
   c. Myocardial dysfunction, pericarditis, vasculitis, coronary abnormality (consists of abnormality in echocardiography, an increase of troponin/NT-pro BNP)
   d. Proven coagulopathy (Increase in PT, APTT, D-Dimer)
   e. Acute symptoms of gastrointestinal (diarrhea, vomiting, or abdominal pain)

AND increase in inflammatory markers such as LED, CRP, or procalcitonin.

AND no prove of involvement of bacterial etiology as the cause of inflammation (bacterial shock, shock due to staphylococcal or streptococcal)

AND with confirmed case COVID-19 infection (RT-PCR, positive antigen test, or positive serology) or high probability of contact with the confirmed case (IDAI, 2020).

Chart 1. Algorithm of Classification COVID-19 case on adult (Andriani, 2020)
The severe and critical case of SARS-CoV-2 patient relates to another disease experienced by the patient (such as, Hypertension) (Dong et al. 2020). The number of COVID-19 case with comorbid in Indonesia reach 1881 with hypertension 52,2%, diabetes mellitus 35,2%, heart diseases 18,4% and others. (Satgas COVID-19, 2020).

Laboratory findings on adult and pediatric of COVID-19 cases

The laboratory findings of child cases in Indonesia have been compared with laboratory findings in Wuhan China. There are 4 studies conducted on lymphocyte range and two studies reported that there is a decrease in lymphocytes for 10 of 214 cases. Based on two other studies which reported there was an increase in lymphocytes for 18 of 43 cases. Besides changes in the number of lymphocytes, there was also a change in the amount of C-Reactive protein that increased (>5mg/L) in 70 of 271 pediatric cases infected with SARS-CoV-2 (Lee-Archer and von Ungern-Sternberg, 2020).

Blood test findings in adult cases infected with SARS-CoV-2 include lymphocyte range, neutrophil count, total cell T, total CD4+, CD8+, total cell B, total cell NK (Natural Killer), and CRP total (C-Reactive Protein). Based on some studies conducted in Wuhan, it is found that there is a decreased amount of white blood cells is (<4x10^9) from 10 of 40 adult cases. Not only the decrease amount of white blood cells, but there is also a decrease amount of lymphocytes in adults from 26 of 40 cases reported the number of lymphocytes is <1.0x10^9/L (Huang et al., 2020). Other studies also compared the immune profile between children and adults that in adults is found a lower amount of cell T, cell T CD8+, and cell B (Chen et al., 2020).

| Table 3. Laboratory results of COVID-19 in pediatric and adults |
|---------------------------------------------------------------|
| **Pediatric** (n=12) | **Adults** (n=20) | **Pediatric** (n=38) | **Adults** (n=41) |
| Neutrophil (x10^9/L) | | 5,6-6,6 | 3,3-8,9 |
| Lymphocyte range (x10^9/L) | | 4,33-6,13 | 0,6-1,1 |
| Hemoglobin (g/L) | | 114-140.15 | 118.0-140.0 |
| Cell T total (x10^9/L) | 2.13 ± 0.72 | 1.06 ± 0.53 | |
| CD4+ cell T (cell/ul) | 598.10 ± 215 | | 425.50 ± 278.10 |
| CD8+ cell T (cell/ul) | 442.50 ± 246.80 | | 117.50 ± 144.10 |
| Cell B Total (x10^9/L) | 194.70 ± 75.42 | 120.9 ± 57.89 | |
| NK Cell (x10^9/L) | 208.2 ± 117.4 | 191.2 ± 87.91 | |
| CRP (mg/L) | 11.51 ± 2.39 | 23.34 ± 2.84 | |

*Source: Chen et al., 2020; Huang et al., 2020; Liu et al., 2020*
Radiological findings in adult and pediatric with COVID-19

Radiological examinations that are often conducted on children infected with COVID-19 are chest x-rays and chest CT scans, both of which often reveal unilateral or bilateral cloudiness. Based on the chest x-rays showed abnormalities in 24 of 46 cases. These abnormalities were in the form of unilateral changes that occurred in 15 of 46 pediatric cases and there were also bilateral changes in 7 of 46 pediatric cases. Besides chest x-rays, there are also chest CT-scans. Based on this examination, it is reported normal from 89 of 267 cases and there were unilateral changes in 63 of 267 cases, and 112 of 267 cases had bilateral changes. Wuhan Children Hospital reported that from 20 pediatric cases of COVID-19, all of them reported sub-pleural changes on chest CT-scans (Lee-Archer dan von Ungern-Sternberg, 2020; Xia et al., 2020).

Some studies also mentioned chest CT-scans and chest x-rays changes reported from 6 of 8 cases that showed bilateral pneumonia and unilateral pneumonia. The changes of image showed there is more than one shadow like a patch in 7 of 8 cases, Ground- Glass opacity in 6 of 8 cases, pleural effusion in 1 of 8 cases, and a white pulmonary appearance was found in 1 of 8 cases (Sun et al., 2020). Based on these results, it is recommended to conduct a CT-scan examination for children infected COVID-19 (Lee-Archer and von Ungern-Sternberg 2020; Xia et al. 2020).

The radiological findings in adult COVID-19 cases were the same as in cases of children. The examinations that are often conducted on adults are x-rays and CT-scans, in 101 cases there were abnormalities on CT-scans such as GGO (86,1%), mixed GGO and consolidation (64%), dilation of blood vessels in the lesion (71,3%), and bronchiectasis (52,5%). There is some lesion that found in CT-scan image in an adult patient that is the peripheral distribution (87%), bilateral (82,2%), and also found multifocal (54,5%) (Zhao et al., 2020).

![Figure 2](image_url) CT-Scan image of two children patients. (A) patient 1 is a 16 years old male with cough symptoms. Based on chest CT-Scan appear GGO image (Ground-Glass Opacity) on the right lungs. (B) patient 2 is a 14 years old female with fever and cough symptoms. Based on CT-Scan appear GGO image (Ground-Glass Opacity) and shadow on the left lungs (Chen et al., 2020).
Immunological response in adult and pediatric cases to COVID-19

SARS-CoV-2 can be high in the lower respiratory tract in early stage. Inflammatory signaling molecules are released by infected cells and alveolar macrophages in addition to recruited T lymphocytes, monocytes and neutrophils. SARS-CoV-2 induce host immune response (Wiersinga, Rhodes, Cheng, Peacock, & Prescott, 2020). Immunization is a way to increase the innate immune function, aiming to make the condition more active after fighting antigens (infection or vaccination) by increasing the Krebs cycle and epigenetic changes such as the transcription of IL-1β, IL-6, and TNF-α genes. The process can affect the progenitor cell lines from myeloid cells and monocyte also local cells such as macrophages in the lungs and dendrite cells (Netea et al., 2020).

Some countries with a BCG vaccination program routinely were reported to have lower morbidity and mortality rates (Aaron et al., 2020; Dhochak et al., 2020). The BCG vaccination is often associated with a decrease in acute upper respiratory tract infection in adults and decreased child mortality, but the BCG effect can only stay in 1-2 years (Dhochak et al., 2020; Wardhana et al., 2011). The immunization conducted in children is measles, rubella, and influenza can give them protection to SARS-CoV-2 infection (Dhochak et al., 2020).

The adaptive immune response also has an essential effect on the patient infected with COVID-19. The number of lymphocytes in pediatric cases COVID-19 were reported varied, it can be decreased or increased, and healthy children had more lymphocytes than adults. The level of lymphocytes can be found more in children’s cases who are often infected with viruses and result in a robust immune system (Cristiani et al. 2020).

It was found that the total lymphocytes, CD4+ and CD8+, T cells helper and T cells memory of patients with severe cases decrease significantly, and as well as severe cases in adults. There is an increase in the number of cytokines, namely IL-2, IL-6, IL-10, and the neutrophil amount, indicating the dysfunctional and excessive adaptive immune response that causes damage to the lungs (Dhochak et al., 2020).

**Figure 3.** Chest CT-Scan image of an adult patient 63 years old with fever and cough symptoms. The CT-Scan showed diffusion bilateral image GGO (Ground-Glass Opacities) (Zhao et al., 2020).
Chart 2. Immunology response in children and adults case of COVID-19  
(Cristiani et al 2020; Dhochak et al. 2020; Wardhana et al. 2011)

Management of adult and pediatric case infected with COVID-19

Tabel 4. Management of COVID-19 in adult and children based on severity

|                | Adult                                      | Children                                  |
|----------------|--------------------------------------------|-------------------------------------------|
| **Asymptomatic** | a) Self isolation at home or prepared public facility for 10 days will monitor primary health care officers by telephone. | a) Self isolation for 14 days monitored by health care facilities |
|                | b) Non-acidic Vitamin C tablets 500 mg / 6-8 hours orally for 14 days and to consume multivitamin (vitamin C, B, E, and zinc) | b) Adequate nutrition                       |
|                | c) If the patient has comorbidities, it is recommended to continue taking regular medication. | c) Practicing health protocol               |
|                | d) Other supportive/complementary medicine registered by BPOM may be given with consideration to patient clinical condition | d) Supportive pharmacotherapy; vitamin C (400 mg/day for age 1-3, 600 mg/day for age 4-8, 1200 mg for age 9-13, and 1800 mg for age 12-18 years old. Zinc 20 mg/day or other supplementation may be considered. |
| **Mild**       | a) Self isolation for maximum of 10 days since the course of illness up to 3 days since the symptoms resolved. They will be monitored by primary health care officers. | a) Outpatient care, Self isolation for 14 days monitored by health care facilities |
|                | b) Adequate nutrition and practicing health protocol | b) Adequate nutrition                        |
|                | c) Symptomatic treatment                    | c) Symptomatic treatment                    |
Staff Department of Anesthesiology and Reanimation of RSUD Dr. Soetomo, Medical Faculty of brain injury requires complicated treatment. Therefore, treatment of diabetes insipidus. Diabetes insipidus in cases of hypernatremia corrections are the keys to the successful main treatments for diabetes insipidus in traumatic severe brain injury.

Adequate hypovolemic, polyuric and polyuria of 300cc/hour urine production and 149mmol/l/day. Surgery, the signs of diabetes insipidus was presented by traffic accident 12 hours before being hospitalized. After transportation to the Emergency Installation (IRD) after experiencing a traffic accident.

Patients with traumatic severe brain injury of Indonesia experience severe brain injury in the United States. There are definitive data on the incidence of diabetes insipidus in the first 2 weeks after the injury. One complication is permanent neurological sequelae. About 85% of mortality rate of up to 50%. About 1.5 million people died from severe traumatic brain injury in Indonesia and 500,000 incidents of neurological permanent disability. Severe brain injury is a fatal condition, with varying rates of mortality from 50%.

The incidence of diabetes insipidus in patients with traumatic severe brain injury does not have accurate data. About 1,500 people died from severe traumatic brain injury in Indonesia annually. About 85% of mortality happens within 2 weeks. One complication is permanent neurological sequelae. About 1,500 people died from severe traumatic brain injury in Indonesia annually. About 85% of mortality happens within 2 weeks. One complication is permanent neurological sequelae. About 85% of mortality happens within 2 weeks. About 1.5 million people died from severe traumatic brain injury in Indonesia and 500,000 incidents of neurological permanent disability. Severe brain injury is a fatal condition, with varying rates of mortality from 50%.

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In this case report, a male, 45 years old, was taken to the hospital due to severe brain injury. The patient was taken to the Emergency Installation (IRD) after experiencing a traffic accident 12 hours before being hospitalized. After transportation to the Emergency Installation (IRD) after experiencing a traffic accident.

### Moderate

| Isolation in hospital | Close monitoring |
|-----------------------|------------------|
| Non pharmacological treatment | Symptomatic treatment |
| Adequate nutrition, fluid maintenance, oxygen therapy, laboratory and radiology monitoring | (Such as antipyretics for fever and pain, adequate nutrition and appropriate rehydration) |
| Pharmacological treatment: Vitamin C 200 -400 mg/8 hours in 100 ml normal saline given through 1 hour intravenously | Intravenous antibiotic. Ceftriaxone 50-100 mg/kg/day and/or azithromycin 10mg/kg if atypical pneumonia is suspected |
| Chloroquine phosphate 500 mg/12 hours orally for 5-7 days or Hydroxychloroquine 400 mg/12 hours in 1st day followed by 400mg/24 hours orally for 5-7 days | Oseltamivir if there is suspicion of co-infections with influenza virus |
| WITH   |   |

<1 years : 3 mg/ kg/ every 12 hours >1 years : Give 30 mg every 12 hours.

b) Patients are advised to take 500 mg/6-8 hours of non-acidic Vitamin C tablets orally for 14 days, multivitamin.

c) Chloroquine phosphate 500 mg/12 hours orally for 5-7 days or Hydroxychloroquine 400 mg/24 hours orally for 5-7 days.

d) Azithromycin 500 mg/24 hours orally for 5 days, and one of the following antivirals drugs (Oseltamivir, alluvia, or favipiravir).

e) Other treatment based on existing comorbid and complication.

f) Other supportive/complementary medicine registered by BPOM may be given with consideration to patient clinical condition.

d) Supportive pharmacotherapy; vitamin C (400 mg/day for age 1-3, 600 mg/day for age 4-8, 1200 mg for age 9-13, and 1800 mg for age 12-18 years old. Zinc 20 mg/day or other supplementation may be considered.
e) Azythromycin 500 mg/24 hours intravenously or orally (5-7 days) OR levofloxacin WITH f) One of the following antiviral: Oseltamivir, alluvia, favipiravir, remdesivir g) Anticoagulant LMWH/UFH h) Other symptomatic treatment i) Other therapy based on existing comorbid and complications

| Severe or critical and MIS-C in children | a) Isolation in hospital | a) Intensive care unit with negative pressure |
|-----------------------------------------|------------------------|--------------------------------------------|
|                                         | b) Full bed rest, adequate nutrition, monitoring for electrolyte level, fluid maintenance, and oxygen | b) Close monitoring and serial laboratory/imaging examination |
|                                         | c) Close monitoring of laboratory parameter and serial thorax imaging | c) Oxygenation, fluid, and adequate nutrition |
|                                         | d) Monitoring for critical condition; respiratory failure, shock, or multi organ failure that need intensive care. | d) Supportive treatment |
|                                         | e) Oxygen therapy; NRM, HFNC, NIV, invasive mechanical ventilation, ECMO | e) Intravenous antibiotic |
|                                         | f) Pharmacotherapy: vitamin C, vitamin B1, phosphate chloride or hydroxychloroquine, azithromycin or levofloxacin, antibiotic based on focal infection, antiviral, anticoagulant, dexamethasone, comorbid and complications management, and other supportive treatment | f) Potential antivirus and hydroxychloroquine may be considered. |
|                                         | g) Plasma convalescens, corticosteroid, anticoagulant, other supplementation | g) Oseltamivir in suspected co-infections with influenza virus |
|                                         | h) Vitamin C, zinc, and other supplementation | h) Vitamin C, zinc, and other supplementation |

Hours for children with weight under 15 kg
Give 45 mg/ 12 hours for children with weight 15 until 23 kg
Give 60 mg/ 12 hours for children with weight 23 until 40 kg
Give 75 mg/ 12 hours for children with weight over 40 kg.

Vitamin C 1 until 3 years 400mg/day 4 until 8 years 600 mg/day 9 until 13 years 1,2 gram/ days 12 until 18 years 1,8 gram/ days

Mortality rate of up to 50%.
About 1.5 million people with severe brain injury in Indonesia so far.

The definitive data on the incidence of diabetes insipidus in patients with traumatic severe brain injury of Indonesia for the first 2 weeks after the injury, which exhibits and the signs of diabetes insipidus was presented by 85% of mortality occurs in the first 2 weeks after the injury.

One of the complications of a severe brain injury is diabetes insipidus.
(Agha and Thompson, 2000).

In the case of being handled improperly, it can bring death.

The initial impact of systemic hypotension and the first 2 weeks after the injury, which exhibits hypernatremia corrections are the keys to the successful treatment of diabetes insipidus.

Adequate hypovolemic, polyuric and plasma abnormalities are marked by the unresponsiveness of hormone (ADH).
Kidney abnormalities is a disease caused by the lower production, is diabetes insipidus.
(Approximately 85% of mortality occurs in the first 2 weeks after the injury).

In the case of being handled improperly, it can bring death.

Diabetes insipidus in cases of brain injury characterized by excessive thirst (polydipsia) and hypernatremia, although the immediate administration of desmopressin, the condition of diabetes is not controlled.

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g) Additional therapy based on individual consideration;
- 1. Convalescent plasma
- 2. Anti IL-6 (tocilizumab)
- 3. Mesenchymal stem cell (MSCs)

Source: Andriani, 2020; IDAI, 2020; WHO, 2020, KEMENKES SEPT 2020

Table 5. COVID - 19 in pediatric and adults review

| No | Source                          | Design               | Sample                | Variable                        | Outcome                      | Conclusion                                           |
|----|---------------------------------|----------------------|-----------------------|---------------------------------|------------------------------|------------------------------------------------------|
| 1. | (Liguoro et al., 2020)          | Systematic Review    | Pediatric n= 7480     | SARS-CoV-2                      | Risk lower than adult        | SARS-CoV-2 infected children is milder               |
| 2. | (Dhochak et al., 2020)          | Review Article       | Pediatric and adults  | Pathophysiology of COVID-19     | Children fare better the adults | Immunization in children provides stronger protection against the SARS-CoV-2 virus so that it can reduce comorbid rates |
| 3. | (Huang et al., 2020)            | Cohort               | Adults n= 41          | Clinical Features               | Risk on adults               | Adults have a rapidly increasing and very high number of cases of death |
| 4. | (Chen et al., 2020)             | Full length article  | Pediatric and adults  | The clinical and immunological on COVID-19 patient | Features of pediatric COVID-19 patient | The immune response to SARS-CoV-2 differs between children and adults. The immune response in children is better than in adults. |
| 6. | (Dong et al, 2020)              | Article Journal      | Pediatric n=2143      | Epidemiology pediatric          | Characteristics of 2149 patient COVID-19 | The clinical manifestations of SARS-CoV-2 which infect children are not as severe as in adult cases |
COVID-19 in children is often caused by infection from family members who live in one house (70-80%) (Setiabudi, 2020). Infected cases are divided into high-risk close contact cases and low-risk close contact cases. The high-risk close contact cases if you have been in contact with a patient OF COVID-19 and the close low-risk contact if you have been in contact with a patient under surveillance (Andarini, 2020).

The treatment given to patients with confirmed of COVID-19 depends on the severity of the case and for cases of children with confirmed of COVID-19, there are several differences where negative pressure isolation, IFN nebulization, and antibiotics and antivirals based on WHO (Andarini, 2020). Treatment antiviral in adult can be given Chloroquine phosphate with dose 500 mg/12 hours orally for 5 days but in children can be given Oseltamivir with dose according to age and weight. Treatment in the critical case may be different with other classification cases. In the critical cases, we should recognize septic shock and ARDS (Acute Respiratory Distress Syndrome); children with critical cases should
receive emergency airway management and oxygen therapy during resuscitation to target \( \text{SpO}_2 \geq 94\% \). Once the patient stable, the use of nasal prongs or nasal cannula is preferred for children. Adult with critical case should receive emergency airway management and oxygen therapy during resuscitation to target \( \text{SpO}_2 \geq 94\% \) (WHO, 2020).

There are more positive confirmed COVID-19 in children in Indonesia with a higher mortality rate than other countries in Asia in particular and the world in general (IDAI, 2020). This leads to the need for comprehensive measures to overcome global pandemic of COVID-19 to reduce the rate of transmission in children and short and long-term adequate treatment. A serious cooperation is needed in every aspects of life from health, education, family, and the environment regarding the dangers and awareness of COVID-19. Studies with COVID-19 confirmed case of children in Indonesia is also needed so can be identified in a more detailed map of transmission, symptoms and long-term treatment.

CONCLUSION

Based on this study, it can be concluded that the case in adults is more severe and have more cases. COVID-19 case happens in a patient who has another medical history such as hypertension and diabetes mellitus. The pediatric case is milder because of the immunization effect and ACE-2 rate, so the difference can be seen from the pathophysiology. The management of pediatric cases and adults have differences in the way of isolation and drug dosage.

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