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Systematic Review

Analysis of Convalescent Plasma Transfusion in Children Confirmed with COVID-19: A Systemic Review

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Abstract

AIM: This study aims to analyze the effectiveness of convalescent plasma therapy in children who are confirmed positive for coronavirus disease-2019. This study focuses on the mechanism of treatment administration and the prognosis after convalescent plasma transfusion.
METHOD: Article searches were conducted using a combination of keywords, namely, "COVID-19," "convalescent plasma," and "children" or "pediatric." Databases used were from Pubmed, ScienceDirect, Wiley Online, Springerlink, and Ebsco and 501 articles were found. The articles submitted are articles with low bias, where the selection of reports follows the inclusion and exclusion criteria according to the Preferred Reporting Items for Systematic Review and Meta-Analysis protocol.
RESULTS: A total of 8 articles were selected. Convalescent plasma transfusion was given to 11 children whose condition worsened starting with signs of tachypnea and decreased saturation, then the children were admitted to intensive care. The dose of convalescent plasma is based on the child's weight. All children had a good prognosis after the transfusion, and 7 children had recovered and were discharged from the hospital.
CONCLUSION: Convalescent plasma transfusion in children who are confirmed positive for coronavirus disease-2019 effectively improves the clinical condition of children. However, it must be noted that the blood from the donor has gone through the correct protocol.
Keywords: Children, convalescent plasma, COVID-19, prognosis

Introduction

A total of 223 countries in the world have been infected with coronavirus disease-2019 (COVID-19) with more than 177 million positive confirmed cases, of which 3.8 million have died. In Indonesia, as of June 20, 2021, there were 1,976,172 confirmed COVID-19 patients and there were 6.9% active cases, of which 2.7% died. Positive cases in children amounted to 12.5% and contributed to the mortality rate of 1.2% (Satgas COVID-19, 2021). The high cases in children are exacerbated by the unclear signs and symptoms of COVID-19 in children. This is because the symptoms are similar to the symptoms of pneumonia. Yayla et al. (2020) studied the symptoms of COVID-19 in children retrospectively from March to June 2020 at the Ankara Turk Hospital. The results showed that 8.6% were positive for COVID-19 out of 2530 children admitted to the hospital with suspected COVID-19. Of all children who were positive for COVID-19, 25.5% were asymptomatic, 5% had mild symptoms, 26.8% had moderate symptoms, and 2.7% had severe symptoms.

The analysis of 41 children aged 0.5–14 years who were tested positive for COVID-19 showed that 30 children were categorized as mild COVID-19, while 11 children had severe COVID-19. This category can be wrong, where a misdiagnosis of COVID-19 in children is most likely due to uncertain symptoms, so a careful assessment of the combination of pediatric clinical, lung x-ray, and viral tests is needed (Zhang et al., 2020). This allows pediatric patients to suddenly be classified as severe because of the misdiagnosis. Severe symptoms will worsen the child's prognosis, where complications of COVID-19 in children may experience delays, and multisystem inflammatory syndrome in children in the form of worsening conditions can occur 3–4 weeks after the child is infected (Baron et al., 2020). In COVID-19 patients with severe symptoms, one of the therapies that can be used is convalescent plasma transfusion.

Convalescent plasma is an antibody-based therapy currently available for the treatment of COVID-19 patients (Joyner et al., 2020). In patients with a history of previous pandemics or other cases of coronavirus resembling pneumonia, convalescent plasma can be used as therapy with good prognosis (Samad et al., 2020; Shen et al., 2020; Teimury & Khaledi, 2020). However, regulations regarding donors can run into obstacles. A total of 7361 people donated by becoming blood donors, but 248 (3.4%)

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of them turned out to be COVID-19 positive during the examination (Slot et al., 2020). So special attention is needed to ensure that blood is not infected with COVID-19, even in difficult situations, the risk of lack of blood bags increases (Tiberghien et al., 2020). Based on this exposure, the effectiveness of convalescent plasma transfusion needs to be studied further by paying attention to the prognosis in children and how the mechanism of convalescent plasma transfusion in cases of COVID-19.

The first Randomized Controls Trials (RCT) study showed that convalescent plasma was not significantly used in COVID-19 patients, but COVID-19 cases with severe symptoms showed good patient progress. Convalescent plasma is a type of blood transfusion obtained from donors who have recovered from COVID-19 (Casadevall et al., 2020). The experience of pediatric nurses while caring for children with COVID-19 patients in the isolation room illustrates that nurses need more effort in carrying out nursing care, especially novelties about both independent and collaborative interventions. The pediatric nurse's effort is due to the confusion of knowledge about COVID-19 itself, while nurses are always near patients (Hastuti et al., 2021).

The role of nurses in collaborative action will be maximized if nurses understand when is the best time to give convalescent plasma to COVID-19 pediatric patients based on the patient's symptoms, as well as nurses themselves who can directly describe the post-intervention prognosis so that they can describe the effectiveness of convalescent plasma in COVID-19 children. The research question is how effective convalescent plasma is in COVID-19 children by taking into account the patient's prognosis and the administration mechanism.

Method

Study Design

This research design is a systematic review used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement indications.

Search Strategy and Study Selection

The process of preparing a systematic review must be systematic, starting from searching for the literature to be used (Pradana et al., 2021). The article search protocol uses Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P). Starting from compiling the protocol, keywords, database used, and the search process until the selected articles are reported using the PRISMA-P mechanism and protocol (Moher et al., 2015). The literature selection included in the process uses the PICO format, namely Problem/Population, Intervention, Comparison, and Outcome (Booth et al., 2016). Problem/Population, Intervention, Comparison, and Outcome in this study is described as follows:

P: The target population in this systematic review is children aged 0–18 years who have tested positive for COVID-19.

I: This systematic review emphasizes the administration of convalescent plasma therapy while the child is hospitalized and the donor used for transfusion.

C: none.

O: The outcomes studied in this systematic review are the prognosis of the child's condition while coming home, dying, or experiencing complications. In addition, the method included in the systematic review is only case study articles.

Article searches were conducted from May to July 2021 using a combination of keywords, namely, "COVID-19," "convalescent plasma," and "children" or "pediatric." The keywords are derived from the PICO strategy created previously, and the search terms have been adjusted and checked against the MeSH terms. Two authors conducted an in-depth article search regarding convalescent plasma transfusion in COVID-19-positive children. Each author used Mendeley software in the article search selection; the first author searched for articles from the ScienceDirect, Wiley Online, and Springerlink databases,

Table 1.
Keyword and Searching Strategy

Databases	Main Search	Limits	Total Articles	Exclusion
PubMed	("COVID-19" OR SARS-CoV-2") AND Convalescent AND ("Children")	English, Full-text, Years 2020–2021	29	26 Excluded based on title/abstract, not intervention of convalescent, non case reports,
Wiley	"COVID-19" AND Convalescent AND Pediatrics OR Children	English, Journals, Last 2 years, Open Access Content,	22	19 Excluded based on title/abstract, not intervention of convalescent, non case reports
ScieneDirect	"COVID-19" AND "Convalescent plasma" AND Pediatrics OR Children	English, Full-text, Years 2020–2021, Research article	297	293 Excluded based on title/abstract, not intervention of convalescent, non case reports
SpringerLink	"COVID-19" AND Convalecent AND Pediatrics OR Children	English, article	97	96 Excluded based on title/abstract, not intervention of convalescent, full text unavailability
CINAHL	("COVID-19" OR SARS-CoV-2") AND "Convalescent plasma" AND Pediatrics OR Children	English, Full-text, Years 2020–2021, academic journal major heading, age: children/pediatrics	56	54 Excluded based on title/abstract, not intervention of convalescent

Note: COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

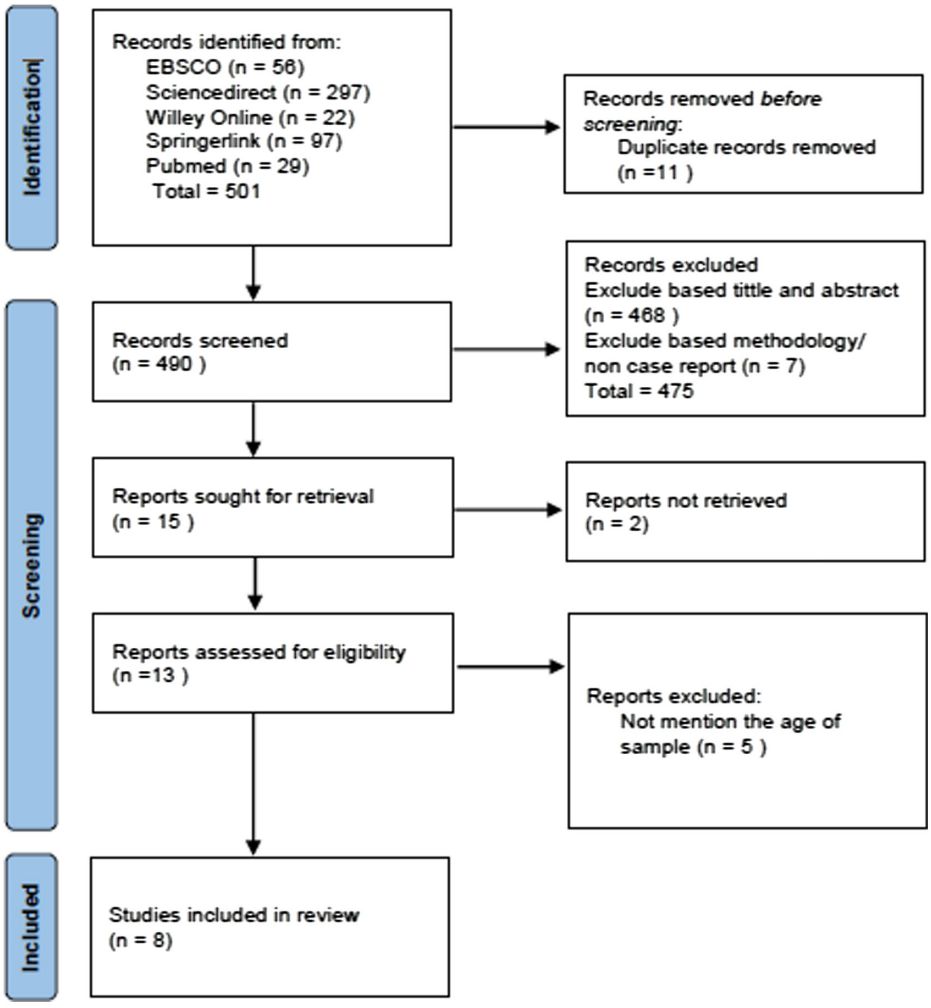

Figure 1.
PRISMA Flow Chart. PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol.

while the second author searched for articles from Pubmed and Ebsco (CHINAHL) database (Table 1). After obtaining full articles from each database, the two authors compiled articles in Microsoft Excel to make sure no selected articles were the same. The search results found 501 articles, then based on the selection using the PRISMA protocol, 8 selected articles were obtained that met the inclusion and exclusion criteria (Figure 1).

Inclusion and Exclusion Criteria

Search articles using inclusion criteria, including (a) articles in English, (b) containing articles on convalescent plasma transfusion in children with COVID-19, (c) articles representing case studies, cohorts, or retrospectives that present cases of convalescent plasma administration in children positive for COVID-19, and (d) limitations are carried out by selecting articles published from 2020 to 2021. Articles that could not be accessed in full text and articles discussing convalescent plasma administration without mentioning the child's age were excluded.

Quality Appraisal

Thirteen articles met the inclusion criteria, but only eight were critically appraised because five other articles were excluded. The first and second authors carried out the critical analysis in a meeting, where the two authors criticized based on eight questions in the checklist form for the case report article Joanna Briggs Institute (Moola et al., 2017). If the two authors are deadlocked to ensure the article is included as the selected article, the third or fourth author becomes the final decision. To see the quality of the selected articles, the author also uses free software on the internet, namely, RevMan Version 5.4.1, to display the risk of bias.

A total of eight selected articles were critically assessed, which were then displayed in the risk of bias. An assessment of the quality of selected articles should be carried out to reduce bias. The assessment of selected articles uses seven question criteria, where the results are marked. Sign "?" means that the criteria in the selected articles are not transparent or there is no information. The "+" sign means that the criteria are found, thereby

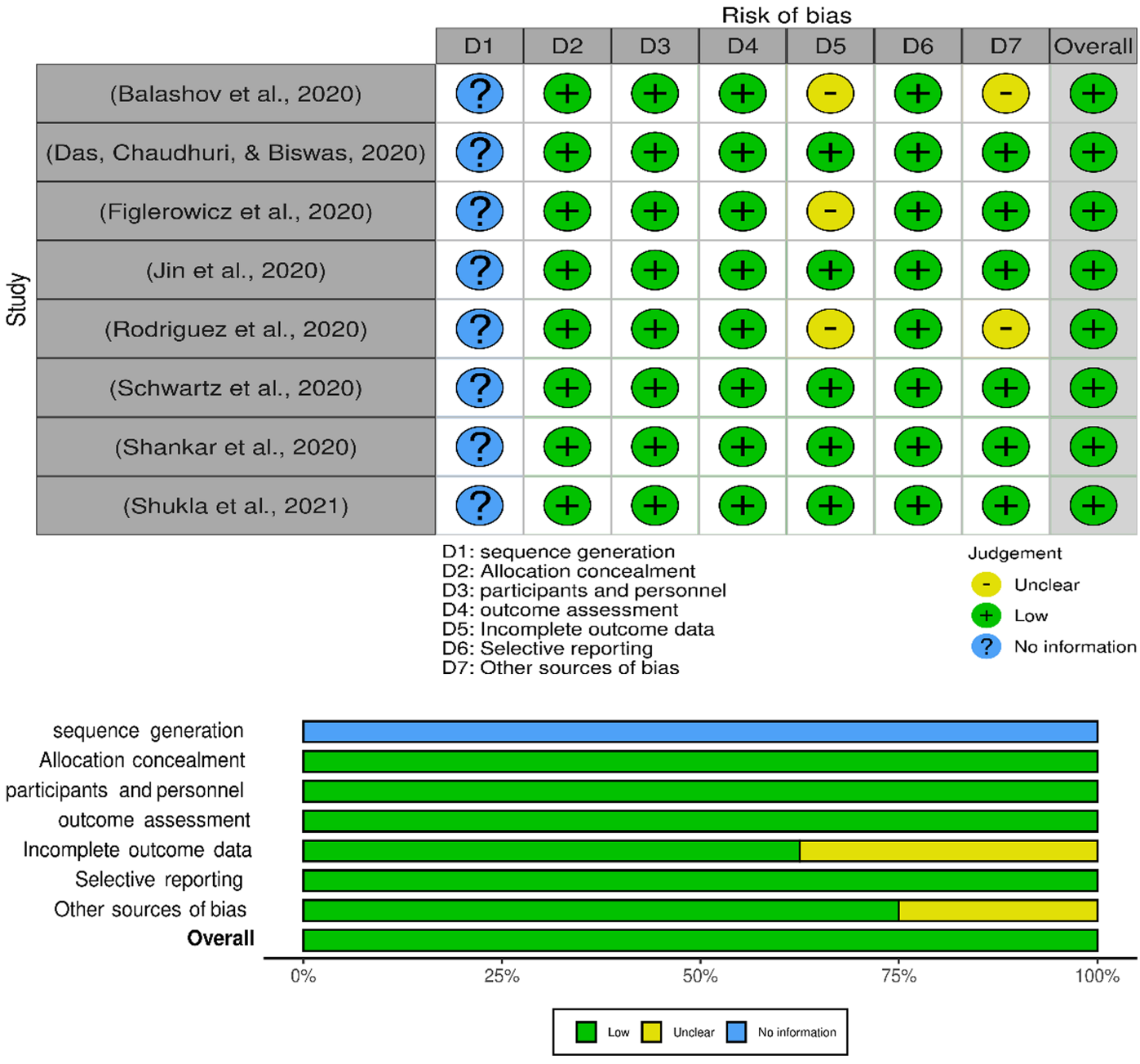

Figure 2.
Risk of Bias Sumary.

reducing the bias, while the "–" sign means that the criteria are not found, thereby increasing the bias. The seven criteria then conclude the quality of each selected article (McGuinness & Higgins, 2021). All selected articles have overalls with a "+" sign, meaning that the risk of bias is low (Figure 2).

Results

Data extraction from each article has been carried out according to the PRISMA-P guidelines. A total of 8 articles were included in the systematic review; from 8 articles, there were 11 case reports of positive COVID-19 children who received convalescent plasma transfusion therapy. All case studies discussed the course of the disease, starting from the initial symptoms when the child was admitted to the hospital, the conditions that became the reason the child received a convalescent plasma transfusion, to the child's prognosis after therapy (can be seen in Table 3). In addition, the mechanism of administration of convalescent plasma therapy, especially dose and titer, was also described. The characteristics of each patient in the case study are given in Table 2. Therefore, this systematic review describes the mechanism of convalescent plasma administration and the prognosis after treatment.

Table 2.
Characteristic of the Patient

Author/Country	Patient Number	Gender	Age	CPT (Titer)	Dose
(Balashov et al., 2020) Russia	1	Female	9 month old	3 times (1:160, 1:160, and 1:80)	10 mL/kgBW
(Das, Chaudhuri, & Biswas, 2020) India	1	Female	13 years old	2 times (1:640)	200 mL/day
(Figlerowicz et al., 2020) Poland	1	Female	6 years old	1 times (1:700)	200 mL
(Jin et al., 2020) USA	1	Male	10 years old	2 times (1:80)	200 mL
(Rodriguez et al., 2020) Italy	1	Female	9 weeks old	2 times (1:126 and <1:50)	7.7 mg/dL
(Schwartz et al., 2020) USA	4	Male	15 years old	2 times (1:160)	2 mL/kgBW
		Male	16 years old	2 times	4 mL/kgBW
		Female	5 years old	1 times (1:1280)	10 mL/kgBW
		Female	12 years old	2 times (>1:2560; 1:640)	4 mL/kgBW
(Shankar et al., 2020) India	1	Female	4 years old	2 times (1:253)	15 mL/ kgBW
(Shukla et al., 2021) India	1	Female	58 days old	1 times (1:80)	50 mL

Mechanism of Convalescent Plasma Administration
Table 2 shows that the dose given to children varies according to the child's weight. For example, the lowest dose of 2 mL/kg BW was given to a boy aged 15 years (Schwartz et al., 2020), while the highest dose of 15 mL/KgBW was given to a girl aged 4 years(Shankar et al., 2020). In addition to convalescent plasma doses, the titers used also vary. For example, the lowest titer was <1 : 50(Rodriguez et al., 2020) and the highest titer was 1 : 2560 (Schwartz et al., 2020).

Prognosis Post-Convalescent Plasma Administration
Table 3 shows 11 cases of COVID-19 children who were given convalescent plasma in 8 selected articles. The convalescent plasma transfusion therapy for the 11 children was the worsening of the condition characterized by tachypnea and decreased oxygen saturation. However, worsening of the condition may also present with other symptoms such as hepatomegaly and atelectasis (Figlerowicz et al., 2020) and atelectasis (Rodriguez et al., 2020). In addition, a history of comorbidities can also be a burden in pediatric patients with COVID-19. The secondary diseases suffered by children include leukemia (Balashov et al., 2020; Figlerowicz et al., 2020; Shankar et al., 2020), trisomy 21 (Rodriguez et al., 2020), and obesity (Schwartz et al., 2020). Meanwhile, the prognosis after convalescent plasma therapy was positive, in which 7 out of 11 children tested negative for reverse transcription-polymerase chain reaction (RT-PCR) and were discharged. At the same time, the other four children showed improvement in their condition with a good prognosis but were still being treated.

Discussion

The dose of convalescent plasma therapy is carried out with reference to the normovolemia principle to avoid the occurrence of Transfusion Associated Circulatory Overload. The recommended dose in children is 10 mL/kgBW (Cao & Shi, 2020). The recommended convalescent plasma dose for children weighing less than 40 kg is 10–15 mL/kgBW (Burhan et al., 2020). The variation in dosage is adjusted to take into account the patient's weight, age, and condition (Triyono & Sukorini, 2020). The dose of convalescent plasma has not been determined, although there are recommendations. The administration is based on the pediatric patient's weight, so the nurse must be able to measure the patient's weight optimally to reduce the risk of dose errors.

Convalescent therapy is one of the treatment options that can be chosen. The principle of giving convalescent plasma therapy is that it uses a passive antibody therapy approach obtained from the plasma of COVID-19 survivors who have been declared cured (Triyono & Sukorini, 2020; Tobian & Shaz, 2020). Antibodies contained in donor plasma are expected to trigger an immune response by neutralizing the virus in the patient's body to increase the cure rate (Triyono & Sukorini, 2020). Although the current research regarding the effectiveness and efficacy of convalescent plasma therapy in children is still limited, passive antibody therapy has been widely used during the SARS-CoV-1, Middle East Respiratory Syndrome (MERS), and Ebola outbreaks (Bloch et al., 2020; Sullivan & Roback, 2020). The ideal conditions that must be met when preparing convalescent plasma therapy in Indonesia include: results of a SARS-CoV-2-specific antibody titer of more than 1/320; antibody titer having virus-neutralizing activity more than 1/80; has passed the screening for The Hepatitis B Virus (HBV), The Hepatitis C Virus (HCV), HIV, and syphilis, and convalescent plasma that has passed the pathogenic inactivation procedure. Convalescent plasma contains a high titer of SARS-CoV-2 antibody to be effective in neutralizing the virus, preventing the infection process in healthy cells, and activating the body's protective mechanisms (Cunningham et al., 2020; Triyono & Sukorini, 2020). The FDA also recommends an effective convalescent plasma titer of >1 : 320 (Center for Biologics Evaluation and Research, 2021). The transfused convalescent plasma should preferably come from a single donor. This is to avoid the risk of infection and alloimmunization reactions (Triyono & Sukorini, 2020). Therapy should be given before the peak phase of viral infection to increase the healing effect on the patient. Research shows that administering convalescent therapy in the third week after disease onset

Table 3.
Chronology of Convascent Plasma Transfusion (CPT) Intervention

Author/Country	Initial Conditions	Reason For Giving CPT	Prognosis
(Balashov et al., 2020) Russia	Children with juvenile myelomonocytic leukemia, day 99 after stem cell transplantation, positive COVID-19 children without clinical or radiological symptoms	The 125th and 144th days showed symptoms of dry cough, shortness of breath, and 94% SaO_2.	Four months after the first COVID-19 detection, the lung of patient was clean of lesion detected by CT scan.
(Das et al., 2020) India	A 13-year-old girl with fever, cough, sore throat for 3 days, difficulty in breathing and restlessness. Pulse rate, 146/minute; BP, 90/58x/minute; RR, 20x/minute; SaO_2 88%. The condition of patient categorized as severe COVID-19.	The child's condition worsened on the second day, ARDS occurred (Hb, 7.3 g/dL; SaO_2 80%), and mechanical ventilation was installed.	On the fifth day, the child's condition improved. On the seventh day, the ventilation was removed and without using breathing apparatus. On the tenth day, the patient recovered and went home.
(Figlerowicz et al., 2020) Poland	The child had a fever, headache, sore throat, and a rash with many small purple dots on the skin, arms, and legs. Three days earlier, the child started feeling tired and had a fever. The temperature was 39°C.	The child has bradycardia (48–50x/minute). Abdominal ultrasound showed hepatomegaly and bilateral renal enlargement (9.8 cm right and 11.5 cm left).	Three weeks later, the test to detect SARS-CoV-2 RNA in nasopharyngeal swabs was performed seven times. All results are negative. The results showed that there were no side effects, and the patient's condition improved.
(Jin et al., 2020) USA	One out of three positive COVID-19 patients are pediatric patients. Symptoms on day 10 are fever, cough, chest pain. X-ray shows pulmonary infiltrates.	The child had a worsening condition on the 19th day of hospitalization.	The child recovered and went home on the 29th day.
(Rodriguez et al., 2020) Italy	Infants with trisomy 21 and AVVR had respiratory failure, hypoxemia, and cardiac decompensation.	On the 8th and 12th days of treatment, the condition worsened again until atelectasis occurred.	The baby began to experience improvement, the 35th day of treatment was extubation, and on the 47th day of hospitalization, the baby was declared hostile for COVID-19 with a good prognosis.
(Schwartz et al., 2020) USA	The first child was obese, had 7 days of fever (40°C), cough, difficulty in breathing, chest pain, nausea and vomiting, do not want to drink. The second child was obese, had 14 days of fever, cough, shortness of breath, rhinorrhea, chest pain, weakness, nausea, and does not want to drink. Third child had 5 days of fever, abdominal pain, dysuria, nausea and vomiting, erythema in the abdomen and chest. Fourth child had 7 days of fever, cough, fatigue, and heavy breathing.	The first and second children, immediately after admission to the PICU, experienced tachypnea and respiratory distress. The third child had ARDS and hypoxia. The fourth child had afebrile and tachypnea. All children were installed High Flow Nasal Cannula (HFNC).	All the children experienced an improvement in their condition and recovered. They were returning after Convalescence Plasma Transfusion (CPT). The first child went home on the 7th day, the second child went home on the 5th day, the third child went home on the 23rd day, and the fourth child went home on the 10th day.
(Shankar et al., 2020) India	Children with standard risk B lineage acute lymphoblastic leukemia, in remission in maintenance therapy (6 mercaptopurine and methotrexate) presented with fever and neutropenia. The child had high fever with mild tachypnea and no signs of localization. Complete blood count showed neutropenia (absolute neutrophil count was 223 cells/μL).	On the fifth day of treatment, the child was found to have tachypnea with bilateral crackles. Respiration Rate (RR) 55x/minute and severe hypoxia (60% oxygen saturation). Children are treated with oxygen 2–3 L/minute with a face mask where oxygen saturation is >95%.	The transfusion episode was smooth, and there were no transfusion reactions. On day 10, the RR improved, breathing and oxygen demand improved, and oxygen therapy was discontinued 4 days later. The patient was discharged on the 18th day of treatment.
(Shukla et al., 2021) India	Infants with fever symptoms, rapid breathing, difficulty breathing, vomiting, refusal to breastfeed for 4 days, and diarrhea. The examination results are temperature, 98.40F; pulse, 152 x/minute; RR, 62 x/minute; BP, 66/30 mmHg; SaO_2 92%–93%. Physical examination revealed dehydration, crepitus of both lungs, and anemia (Hb, 6.93 mg/dL). X-ray shows pulmonary infiltrates.	On the third and tenth days, the patient received a Packed Red Cells (PRC) transfusion of 10 mg/dL. The condition did not improve, hence, on the fouth day of hospitalization, the baby received convalescent plasma.	After the transfusion, on the second day, the baby improved; on the seventh day, the baby's RT-PCR result was negative, and the baby was sent home on the tenth day.

Note: SaO_2 = oxygen saturation as measured by blood analysis; BP = blood pressure; Hb = hemoglobin; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; PICU = pediatric intensive care unit; AVVR = atrioventricular valve regurgitation; RT-PCR = reverse transcription polymerase chain reaction.

improves patient recovery (Long et al., 2020). The convalescent plasma given to the patient needs to be considered by the nurse, where the nurse must do a double-check and ensure that the plasma titer is appropriate or not too low, preferably above 320.

One of the challenges in adapting to the COVID-19 pandemic in children is the signs and symptoms of COVID-19 in children that resemble signs of pneumonia, some even COVID-19-positive children do not show symptoms (Nasution et al., 2021). Yayla et al. (Yayla et al., 2020) which stated that the most common symptoms in children who were confirmed positive for COVID-19 were fever (40.5%), cough (35.9%), and sore throat (16.8%).

This makes it a disadvantage to determine whether the child is infected with the virus or not. Indonesia implements early detection of COVID-19 with GeNose, rapid antibody, and antigen swab. GeNose is an examination by exhaling into an airbag, and the air is examined for elements of viral compounds. Rapid antigen itself is an examination by taking blood to see whether immunoglobulin (Ig)G and IgM antibodies are formed which indicate an infection in the body. An antigen swab is an examination through the nose, where the swab from the nose is examined to determine the detection of foreign body or part of the virus. However, these three tests are only for initial detection, which is used as a benchmark for the examination in RT-PCR. This RT-PCR swab in the nose and throat is to detect the DNA of the COVID-19 virus.

Convalescent plasma transfusions can be given to children who experience exacerbations and critical symptoms due to being infected with COVID 19. The agreed critical symptom criteria include respiratory failure conditions requiring ventilator assistance, shock, and multiple organ failure (Shen et al., 2020). Criteria for critical symptoms in children in Indonesia include patients experiencing rapid worsening of respiratory failure or developing shock, encephalopathy, myocardial damage or heart failure, coagulopathy, acute renal impairment, and multiple organ dysfunction or other manifestations of sepsis (Burhan et al., 2020). Children who have criteria to fall into the critical symptom phase include children who are in contact with critical COVID-19 patients, patients who have diseases (congenital heart disease, lung and airway disease, acute/chronic kidney disease, malnutrition, neoplasm, diabetes, immunodeficiency, congenital metabolic disease, and others), patients receiving long-term immunosuppressant therapy, and infants younger than 3 months of age (Shen et al., 2020). Based on these findings, nurses can recommend giving convalescent plasma to pediatricians if the child experiences worsening of the condition during hospitalization; the worsening of this condition is related to acute symptoms in the child.

Convalescent plasma is obtained from selected donors according to certain conditions. The first donor requirement that must be fulfilled is someone who has been positive for COVID-19 and has been declared cured, which is at least 2 weeks after the RT-PCR test results are negative and without symptoms. The criteria for recovery are given as follows: normal body temperature for 7 days, normal breathing, no pulmonary infiltrates, RT-PCR twice was negative in 24 hours. There are other criteria besides the requirement to recover, including prospective donors aged 18–55 years and not having COVID-19 symptoms (Li et al., 2020). The mechanism of convalescent plasma donors is adjusted to the ABO blood group, but for special conditions, it is possible for donors with blood type O to donate convalescent plasma to patients with blood group other than O. This is from the results showing that anti-A IgG in blood group O with titer >1:16 is about 70% (Focosi, 2020). One donor can give 2-3 units of convalescent plasma to more than one COVID-19 patients (Casadevall et al., 2020).

The role of nurses is essential in the recovery of COVID-19 pediatric patients, where nurses are health workers who are beside the child 24 hours a day while the child is being treated in an isolation room. Nurses can recognize critical conditions in children as early identification of convalescent plasma administration, even when convalescent plasma is given. Nurses need to pay attention to the dose based on the patient's weight and report the child's prognosis after convalescent plasma administration. So that delays and imprecision of convalescent plasma administration can be avoided.

Study Limitations

This article aims to analyze the effectiveness of convalescent plasma transfusion in COVID-19 children. The limitations of RCT studies related to convalescent plasma in COVID-19, especially in pediatric patients, made the authors take case report articles. However, the review has clearly explained that all pediatric patients in the case report have a good prognosis after convalescent plasma administration. Several limitations were found, including the variety of early symptoms of COVID-19 pediatric patients or the absence of the type or type of COVID-19 virus shown in the case reports studied. However, this is an opportunity for nurses to determine critical conditions with almost the same symptoms in each patient, namely, the worsening of conditions in the respiratory system. Common criticisms may also be questioned; the absence of a PROSPERO registration number or the authors' bias measurement instrument may be different. The author has tried to select a review protocol and all instruments that are most suitable for the case report. Further research on convalescent plasma intervention in COVID-19 children needs to be developed, especially in clinical trials, which of course, involve nurses.

Conclusion and Recommendations

Giving convalescent plasma transfusions to children who are confirmed positive for COVID-19 has been shown to be effective in reducing the deterioration in children. After administration of convalescent plasma, the child's clinical prognosis improved. Convalescent plasma can be given if the child is in a critical condition, that is symptoms of shock, multi-organ failure ,or the installation of a ventilator. Giving convalescent transfusion to children provides antibodies that have been obtained from donors and can trigger antibodies in children. Therefore, there are a number of conditions that must be met by convalescent plasma donors, including being declared cured of COVID-19 with a negative RT-PCR test in two tests in 24 hours;

not currently showing symptoms of COVID-19, either fever or coughing runny nose, and should be checked for antibodies, where the titer result must be more than 1 : 320 (equivalent to a virus neutralization titer of 1 : 80).

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References

Balashov, D., Trakhtman, P., Livshits, A., Kovalenko, I., Tereshenko, G., Solopova, G., Petraikina, E., Maschan, A., & Novichkova, G., Maschan, A., & Novichkova, G. (2021). SARS-CoV-2 convalescent plasma therapy in pediatric patient after hematopoietic stem cell transplantation, *Transfusion and Apheresis Science* , *60*(1), 1–4. [CrossRef]

Baron, M., Sherwen, O., Heaton, P. A., & Paul, S. P. (2020). COVID-19 complications in children. *British Journal of Nursing*, *29*(20), 1146. [CrossRef]

Bloch, E. M., Shoham, S., Casadevall, A., Sachais, B. S., Shaz, B., Winters, J. L., van Buskirk, C., Grossman, B. J., Joyner, M., Henderson, J. P., Pekosz, A., Lau, B., Wesolowski, A., Katz, L., Shan, H., Auwaerter, P. G., Thomas, D., Sullivan, D. J., Paneth, N., Gehrie, E., et al. (2020). Deployment of convalescent plasma for the prevention and treatment of COVID-19. *Journal of Clinical Investigation*, *130*(6), 2757–2765. [CrossRef]

Booth, A., Sutton, A., & Papaioannou, D. (2016). *Systematic approaches to a successful literature review* (2nd ed). London: Sage Publications.

Burhan, E., Susanto, A. D., Nasution, S. A., Ginanjar, E., Pitoyo, W., Susilo, A., … Sambo, M. (2020). *Pedoman Tatalaksana COVID 19* (Edisi. *3*). Jakarta: Perhimpunan Dokter Paru Indonesia (PDPI), Perhimpunan Dokter Spesialis Kardiovaskuler Indonesia (PERKI), Perhimpunan Dokter Spesialis Penyakit Dalam Indonesia (PAPDI), Perhimpunan Dokter Anestesiologi dan Terapi Insentif Indonesia (PERDATIN).

Cao, H., & Shi, Y. (2020). Convalescent plasma: Possible therapy for novel coronavirus disease 2019. *Transfusion*, *60*(5), 1078–1083. [CrossRef]

Casadevall, A., Joyner, M. J., & Pirofski, L. A. (2020). A randomized trial of convalescent plasma for COVID-19 — Potentially hopeful signals. *JAMA*, *324*(5), 455–457. [CrossRef]

Center for Biologics Evaluation and Research (2021). *Investigational COVID-19 convalescent plasma-Emergency INDs*. Rockville, Maryland, United Stated America. Retrieved from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/investigational-covid-19-convalescent-plasma

Cunningham, A. C., Goh, H. P., & Koh, D. (2020). *Treatment of COVID-19: Old tricks for new challenges*. Berlin: Springer.

Cura Yayla, B. C., Özsürekçi, Y., Aykaç, K., Derin Oygar, P., Laçinel Gürlevik, S., İlbay, S., Kukul, M. G., Karahan, S., Cengiz, A. B., & Ceyhan, M. (2020). Characteristics and management of children with covid-19 in Turkey. *Balkan Medical Journal*, *37*(6), 341–347. [CrossRef]

Das, S. S., Chaudhuri, K., & Biswas, R. N. (2020). Successful convalescent plasma therapy in a child with severe coronavirus disease. *Indian Pediatrics*, *1*(12), 1–3.

Figlerowicz, M., Mania, A., Lubarski, K., Lewandowska, Z., Wojciech, S., Derwich, K., Wachowiak, J., & Mazur-melewska, K. (2020). First case of convalescent plasma transfusion in a child with COVID-19- associated severe aplastic anemia. *Transfusion and Apheresis Science, Published:July 01, 2020*, *06*, 1–3. [CrossRef]

Focosi, D. (2020). Anti-A isohaemagglutinin titres and SARS-CoV-2 neutralization: Implications for children and convalescent plasma selection. *British Journal of Haematology*, *190*(3), e148–e150. [CrossRef]

Hastuti, D., Rudhiati, F., & Suryaningsih, C. (2021). The role of pediatric nurses in caring for children with Covid 19 in Indonesia. *Jurnal Keperawatan Komprehensif*, *7*(1), 79–89. [CrossRef]

Jin, H., Reed, J. C., Liu, S. T. H., Ho, H. E., Lopes, J. P., Ramsey, N. B., Waqar, O., Rahman, F., Aberg, J. A., Bouvier, N. M., Cunningham-Rundles, C., & Mount Sinai Health System Convalescent Plasma Team, (2020). Three patients with X-linked agammaglobulinemia hospitalized for COVID-19 improved with convalescent plasma. *Journal of Allergy and Clinical Immunology. in Practice*, *8*(10), 3594–3596.e3. [CrossRef]

Joyner, M. J., Wright, R. S., Fairweather, D., Senefeld, J. W., Bruno, K. A., Klassen, S. A., Carter, R. E., Klompas, A. M., Wiggins, C. C., Shepherd, J. R., Rea, R. F., Whelan, E. R., Clayburn, A. J., Spiegel, M. R., Johnson, P. W., Lesser, E. R., Baker, S. E., Larson, K. F., Ripoll, J. G., Andersen, K. J., et al. (2020) Early safety indicators of COVID-19 convalescent plasma in 5000 patients. *Journal of Clinical Investigation*, *130*(9), 4791–4797. [CrossRef]

Li, L., Tong, X., Chen, H., He, R., Lv, Q., Yang, R., Zhao, L., Wang, J., Xu, H., Liu, C., Chen, G., Chen, S., Li, C., Qiao, J., Yang, J., Wu, Y., & Liu, Z. (2020). Characteristics and serological patterns of COVID-19 convalescent plasma donors: Optimal donors and timing of donation. *Transfusion*, *60*(8), 1765–1772. [CrossRef]

Long, Q., Deng, H., Chen, J., Hu, J., Liu, B., Liao, P., … Xu, Y. (2020). Antibody responses to SARS-CoV-2. In *COVID-19 patients: The perspective application of serological tests in clinical practice*. MedRxiv. https://www.medrxiv.org/content/10.1101/2020.03.18.20038018v1.full.pdf

McGuinness, L. A., & Higgins, J. P. T. (2021). Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Res Syn Meth. Research Synthesis Methods*, *12*(1), 55–61. [CrossRef]

Moher, D., Shamseer, L., Clarke, M., Ghersi, D., Liberati, A., Petticrew, M., Shekelle, P., Stewart, L. A., & PRISMA-P Group (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*. BioMed Central, *4*, 1. [CrossRef]

Moola, S., Munn, Z., Tufanaru, C., Aromataris, E., Sears, K., Sfetcu, R., … Mu, P.-F. (2017). Chapter 7. Systematic reviews of etiology and risk. In E. Aromataris & Z. Munn (Eds.). *Joanna Briggs institute reviewer's manual*. The Joanna Briggs Institute. http://joannabriggs.org/research/critical-appraisal-tools.html

Nasution, L. A., Pradana, A. A., & Casman (2021). Vulnerable populations' coping in facing challenges during the covid-19 pandemic: A systematic review. *Enfermeria Global*, *20*(3), 612–621. [CrossRef]

Pradana, A. A., Chandra, M., Fahmi, I., Casman, R., A. F., Dewi, N. A., & Nuraini (2021). Telaah Literatur sebagai Alternatif Tri Dharma Dosen: Bagaimana tahapan penyusunannya? *JIKDI*, *01*(01), 6–15.

Rodriguez, Z., Shane, A. L., Verkerke, H., Lough, C., Zimmerman, M. G., Suthar, M., Wrammert, J., MacDonald, H., Wolf, M., Clarke, S., Roback, J. D., Arthur, C. M., Stowell, S. R., & Josephson, C. D. (2020). COVID-19 convalescent plasma clears SARS-CoV-2 refractory to remdesivir in an infant with congenital heart disease. *Blood Advances*, *4*(18), 4278–4281. [CrossRef]

Samad, N., Sodunke, T. E., Al Banna, H. A., Sapkota, A., Fatema, A. N., Iskandar, K., Jahan, D., Hardcastle, T. C., Nusrat, T., Chowdhury, T. S., & Haque, M. (2020). Convalescent plasma therapy for management of COVID-19: Perspectives and deployment in the current global pandemic. *Risk Management and Healthcare Policy*, *13*, 2707–2728. [CrossRef]

Satgas COVID-19 (2021). *Satuan Tugas Penanganan COVID-19*. Peta Sebaran. Retrieved from https://covid19.go.id/peta-sebaran

Schwartz, S. P., Thompson, P., Smith, M., Lercher, D. M., Rimland, C. A., Bartelt, L., Park, Y. A., Weiss, S., Markmann, A. J., Raut, R., Premkumar, L., Kuruc, J., & Willis, Z. (2020). Convalescent plasma therapy in four critically ill pediatric patients with coronavirus disease 2019: A case series. *Critical Care Explorations*, *2*(10), (e0237), 1–7. [CrossRef]

Shankar, R., Radhakrishnan, N., Dua, S., Arora, S., Rana, M., Kumar, D., Rai, S., & Gupta, D. K. (2020). Convalescent plasma to aid in recovery of COVID-19 pneumonia in a child with acute lymphoblastic leukemia.

Transfusion and Apheresis Science, Published:September 24, 2020, 1–3. [CrossRef]

Shen, K. L., Yang, Y. H., Jiang, R. M., Wang, T. Y., Zhao, D. C., Jiang, Y., Lu, X. X., Jin, R. M., Zheng, Y. J., Xu, B. P., Xie, Z. D., Liu, Z. S., Li, X. W., Lin, L. K., Shang, Y. X., Shu, S. N., Bai, Y., Lu, M., Lu, G., Deng, J. K., et al. (2020). Updated diagnosis, treatment and prevention of COVID-19 in children: Experts' consensus statement (condensed version of the second edition). *World Journal of Pediatrics* , *16*(3), 232–239. [CrossRef]

Shukla, U., Bhakhri, B., Arora, S., Jain, M., Jain, V., Dua, S., Singh, D. K., & Gupta, D. K., & Gupta, D. K. (2021). Use of convalescent plasma for managing severe COVID-19 infection in 2-month-old infant. *ISBT Science Series*. International Society of Blood Transfusion, *16*(1), 102–105. [CrossRef]

Slot, E., Hogema, B. M., Reusken, C. B. E. M., Reimerink, J. H., Molier, M., Karregat, J. H. M., IJlst, J., Novotný, V. M. J., van Lier, R. A. W., & Zaaijer, H. L. (2020). Low SARS-CoV-2 seroprevalence in blood donors in the early COVID-19 epidemic in the Netherlands. *Nature Communications*, *11*(1), 5744. [CrossRef]

Sullivan, H. C., & Roback, J. D. (2020). Convalescent plasma: Therapeutic hope or hopeless strategy in the SARS-CoV-2 pandemic. *Transfusion Medicine Reviews*, *34*(3), 145–150. [CrossRef]

Teimury, A., & Mahmoodi Khaledi, E. M. (2020). Current options in the treatment of covid-19: A review. *Risk Management and Healthcare Policy*, *13*, 1999–2010. [CrossRef]

Tiberghien, P., de Lamballerie, X., Morel, P., Gallian, P., Lacombe, K., & Yazdanpanah, Y. (2020). Collecting and evaluating convalescent plasma for COVID-19 treatment: Why and how? *Vox Sanguinis*, *115*(6), 488–494. [CrossRef]

Tobian, A. A. R., & Shaz, B. H. (2020). Earlier the better : Convalescent plasma. *Blood*, *136*(6), 652–654. [CrossRef]

Triyono, T., & Sukorini, U. (2020). *Seputar Transfusi Darah Saat pandimu Covid 19: Frequently asked question (FAQ)*. Yogyakarta: Departemen Patologi Klinik dan Kedokteran Laboratorium Fakultas Kedokteran, KMK Universitas Gadjah Mada.

Zhang, Y., Xie, R. M., He, Y. L., Xing, L. H., Dong, L., Zhang, J. Z., Xing, W. H., Lv, X. Y., Lu, Y. B., Liu, Q., Lin, L. B., Liu, G. Z., Li, L., Li, P., Xie, Y. Z., Ni, Z. Y., Yin, X. P., Li, H. J., & Gao, B. L. (2020). Clinical and imaging features of pediatric COVID-19. *Italian Journal of Pediatrics*, *46*(1), 153. [CrossRef]