



# Relapsing Nephrotic Syndrome Associated with COVID-19

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## ABSTRACT

An 8-year and 2-month-old girl presented with generalized edema for two days with a mild cough and shortness of breath. She was diagnosed with a relapsing nephrotic syndrome (NS) and Community Acquired Pneumonia due to a COVID-19 infection. The patient was discharged with complete remission NS and repeated negative PCR for SARS-CoV-2 from nasopharyngeal swabs. It is important to consider COVID-19 infection as a likely trigger of relapsing NS in children.

**Keywords:** COVID-19, relapsing nephrotic syndrome

## ABSTRAK

Seorang anak perempuan usia 8 tahun 2 bulan masuk rumah sakit dengan keluhan edema anasarka selama 2 hari disertai batuk ringan dan sulit bernapas. Diagnosis adalah sindrom nefrotik relaps, pneumonia COVID-19, dan malnutrisi. Pasien dipulangkan setelah sindrom nefrotik remisi dan hasil PCR SARS-CoV-2 negatif. Infeksi COVID-19 penting dipertimbangkan sebagai pencetus relaps sindrom nefrotik. **Jusli Aras, Andi Utari Dwi Rahayu, Husein Albar. Sindrom Nefrotik Relaps pada Infeksi COVID-19**

**Kata kunci:** COVID-19, sindrom nefrotik relaps



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## INTRODUCTION

Nephrotic syndrome (NS) is an illness of protein leakage into the urine, resulting in hypovolemia, hypercoagulation, and infection. The cumulative prevalence of NS in children in USA and Europe has been estimated to be 16 per 100,000 children. In contrast, the incidence in developing countries is approximately 2 – 4 per 100,000 per year and 6/100,000 in Indonesia.<sup>1-4</sup> Most cases with minimal change NS are steroid sensitive with benign prognosis; however, some may develop frequent relapses and a long course of illness, leading to a risk of life-threatening infections, thromboembolic complications, and side effects of long term therapy.<sup>5-7</sup> In developing countries, infections are still a severe problem in nephrotic children, potentially a significant cause of morbidity and mortality.<sup>8-10</sup>

SARS-CoV-2 infection is COVID-19, first occurred in Wuhan, China, and rapidly disseminated globally to cause a pandemic; and observed in approximately 1% of children younger than ten years<sup>11,12</sup> up to 2% of children aged 0–19 years.<sup>13</sup> Figures reported

in Italy, USA, and Spain were approximately 1.2%,<sup>14</sup> 1.7%,<sup>15</sup> and 0.47%<sup>16</sup> respectively. Patients with primary or secondary glomerular diseases on immunosuppressive therapy may potentially be at high risk for COVID-19 due to immunosuppressed states.<sup>17</sup>

## Case

NH, 8 year and 2 months – old girl, was hospitalized due to general edema for two days. She presented with a mild cough and shortness of breath two days before admission and fever for four days. No signs and symptoms of sore throat, nausea, abdominal pain, diarrhea, headaches, and muscle ache, and no clear history of SARS-CoV-2 contact. Her NS has been treated with an oral prednisone regimen since 2019 and followed up regularly.

Physical examination revealed malnutrition with a body weight of 24 kg and a height of 127 cm. Body temperature, pulse rate, respiratory rate, and upper extremity blood pressure were 36,9oC, 98 per minute, 40 per minute, and 100/60 mmHg, respectively. No abnormal findings were observed on the pharynx and

tonsils. Heart auscultation was normal, with mildly reduced breath sounds and rales heard over the lungs. Edema was found in palpebrae, face, and pretibial; also ascites. Other physical findings were unremarkable.

Laboratory studies showed haemoglobin 14.1 g/L, haematocrit 41%, leukocytes 9.900/mm<sup>3</sup> with 40.3% neutrophil, 52,2% lymphocyte, 5,4% monocyte, 1,9% eosinophil, 0,2% basophil, absolute lymphocyte count (ALC) 5167, neutrophil-to-lymphocyte ratio (NLR) 0.77, and platelet 617.000/mm<sup>3</sup>, albumin 0.7 g/dL, C-reactive protein 15.2 mg/dL, procalcitonin 0.28 ng/mL, SGOT 20 U/L, SGPT 22 U/L, and total cholesterol 460 mg/dL. Urinalysis showed a proteinuria of 4+ (1 g/L), trace erythrocytes without leukocytes and absence of glucosuria. Chest X-ray and CT Scan showed consolidation, scattered ground glass opacities over the lungs, pleural effusion, and was diagnosed radiologically as bilateral pneumonia, typical for viral SARS-CoV-2 pneumonia (Figure 1 & 2).

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## LAPORAN KASUS



She was diagnosed with relapsing NS, and community acquired pneumonia was suspected of COVID-19 and malnutrition. She was then referred to the isolation room and treated according to WHO COVID-19 guidelines.<sup>13</sup> She was isolated and treated with oxygen 2 L/min nasal, 75 mL of 20% albumin transfusion with 15 mL furosemide (1 mg/kg) pre and post transfusion, intravenous ceftriaxone 750 mg and gentamicin 40 mg every 12 hours, prednisone 30 mg/day, and nutritional support for malnutrition with 2000 kcal of soft food and full cream milk containing protein 15 g/day, and low salt diet. The patient was consulted to a pediatric pulmonologist for pneumonia.

### Clinical Course

On the fourth day, she appeared weak with a cough, dyspnea, general edema, subcostal retraction, reduced breath sounds, and rales. Serum albumin was 0.9 g/dL after albumin infusion. The medical interventions were continued with nasal oxygen 2 L/minute, intravenous ceftriaxone 750 mg and gentamycin 40 mg every 12 hours, intravenous albumin 20% 75 mL, oral prednisone 30 mg per day, oral furosemide 20 mg every 12 hours, and nutritional support therapy for malnutrition. The PCR result indicated SARS CoV2 infection (COVID-19).

On day 7, she looked well with reduced clinical features, and serum albumin increased to 1.1 g/dL. On day 11, she has no remarkable signs and symptoms. PCR test for SARS CoV2 was negative, and all other laboratory findings were within normal limits. The patient was discharged with the final diagnosis of Community Acquired Pneumonia due to COVID-19 infection, relapsing NS, and malnutrition. The prognosis was favorable; NS remission was achieved as COVID-19 recovered.

### Case Analysis

Nephrotic syndrome (NS) is classically defined as massive proteinuria (>40 mg/m<sup>2</sup>/hr), hypoalbuminemia (<2.5 g/dL), generalized edema, and hyperlipidemia in most cases.<sup>18</sup> Our case was diagnosed as NS due to proteinuria 4+ or 1 g/L, serum albumin 0.7 g/dL, generalized edema, and hypercholesterolemia 460 mg/dL.

Immunosuppressive conditions such as



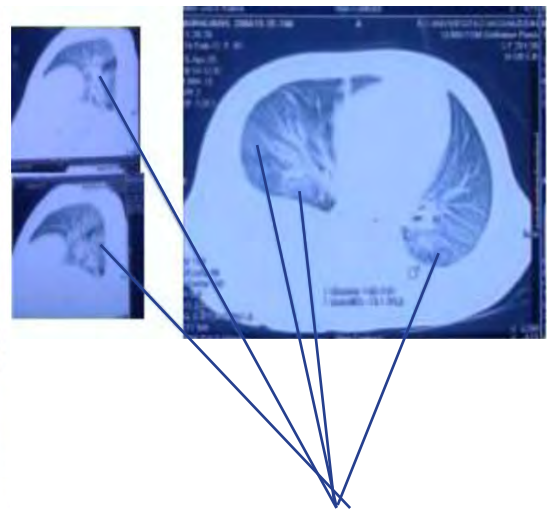
**Figure 1.** Consolidation on the lungs.  
(Source: personal documentation)

long-term steroid therapy are one of the risk factors for COVID-19 infection.<sup>19</sup> It is currently recognized that at least 50% NS relapses are triggered by a viral upper respiratory tract infection.<sup>20-22</sup> may be due to cytokine release.<sup>21,23</sup> Our cases with relapsing NS and long-term prednisone therapy are vulnerable to infection, including COVID-19.

The patient's result of the PCR nasopharyngeal swab test was positive for COVID 19; she was diagnosed with pneumonia due to a COVID-19 infection. The incubation period of COVID-19 infection in children is 1-14 days, usually 3-7 days, with milder symptoms or even asymptomatic, faster recovery, and with better prognosis.<sup>24,25</sup>

Major infections frequently result in relapsing NS, most commonly in the upper respiratory tract, including viral respiratory illnesses such as adenovirus or influenza. We consider the relapse due to COVID-19 infection because the patient was previously in remission and relapsed only after the onset of community-based pneumonia. This is the first reported case of relapsing nephrotic syndrome accompanied by the onset of COVID-19 in Makassar, South Sulawesi; whether the nephrotic syndrome and COVID-19 were coincidental or the relapse was induced by COVID-19 infection is not known.

According to the WHO-China joint report,



**Figure 2.** Signs of ground glass opacities over the lungs.  
(Source: personal documentation)

COVID-19 in children were commonly identified through contact tracing in the households of infected adult,<sup>26</sup> and household contact is a major transmission route in people who lived in the same home with COVID-19 patient, approximately six times more than other close contacts (OR 6).<sup>30</sup> In this case, a history of contact with infected COVID-19 people was denied.

Oral prednisone was continued for NS therapy by the recommendation of National Health Institute.<sup>27</sup> Melgosa M, *et al*, also reported their SARS-CoV-2 patients remained to receive prednisone.<sup>28</sup> Similar finding was also observed in our patient, who recovered with oral prednisone, antibiotics, and other additional supportive therapy.

SARS-CoV-2 became negative in this patient after recovering Community Acquired Pneumonia and NS. COVID-19 infection was considered a trigger for NS relapse in our patient because the clinical and laboratory findings of NS were also improved as her COVID-19 infection was recovered.

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## LAPORAN KASUS



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