

CHAPTER I

INTRODUCTION

1.1 Background

Coronavirus disease-19 (COVID-19) is a contagious infectious disease that is becoming a worldwide problem and has spread. The disease was first detected at the end of 2019 in Wuhan, China, with the alleged spread of the virus from animals to humans for the first time in the Huanan seafood market. COVID-19 has a very broad spectrum of symptoms with characteristics such as fever, sore throat, fatigue, cough and shortness of breath. (World Health Organization, 2021) The incubation period for COVID-19 is 1-14 days; most often 4-5 days. COVID-19 has a broad spectrum of symptoms, ranging from asymptomatic to severe symptoms, namely respiratory failure. Research shows 81% of patients were asymptomatic or with mild pneumonia symptoms, 14% of cases had severe symptoms, including shortness of breath to hypoxia, 5% of cases with critically ill disease, such as respiratory failure, shock, to multiorgan dysfunction. Pneumonia is a clinical manifestation. the most frequently. Symptoms can include fever, cough, shortness of breath, and an infiltrate picture on the chest X-ray. (Syam *et al.*, n.d.) Confirmation of COVID-19 is established through real-time RT-PCR examination. Several other tests can also support the diagnosis of COVID-19. (Zu *et al.*, 2020) It has been reported that the exposure to SARS-CoV-2 virus in pediatric patients can lead to a multisystem inflammatory syndrome in children (MIS-C) that can potentially resulting in multi-organ damage, dysfunction and death. (Esposito and Principi, 2021)

Acute kidney injury (AKI) is a complication of COVID-19 and the pathophysiology of AKI in COVID-19 could be determined as multi-factor.

COVID-19 infection targets Angiotensin Converting Enzyme 2 (ACE2) which triggers angiotensin dysregulation, resulting in the activation of innate immune pathways, adaptive immune pathways, and subsequent hypercoagulation cause organ damage and lead to acute renal failure. (Głowacka *et al.*, 2021) COVID-19 also targets lymphocyte cells that trigger ACE2 expression, which leads to lymphocyte activation resulting in cell death due to induction of activation which can lead to lymphopenia. Innate immune system and coagulation pathways are closely related. In cases of COVID-19 related with macrophages, cytokine storm, and release of molecular patterns due to pathogens and damaged molecular proteins can result in the release of tissue factors and activation of coagulation factors tend to cause hypercoagulability. (Batlle *et al.*, 2020). However, other factors found in similar diseases have also been described, including hypovolemia, heart failure (right and left), sepsis, and dehydration. (Piko *et al.*, 2022) The exact prevalence of AKI in pediatric COVID-19 patients is unknown. Although, some study reports a low incidence rate, but with a more thorough data collection, the incidence of AKI appears to be even higher. In a cohort of 52 children in the United Kingdom, 46% had serum creatinine above the upper limit of normal and 29% met the definition of AKI, but did not require a Renal Replacement Therapy. In another multicentre study, 18% of children critically ill with COVID-19 had AKI. (Kari *et al.*, 2021)

Acute kidney injury or Acute Kidney Injury (AKI) can be defined as a rapid and sudden or severe decrease in renal filtration function. This condition is usually characterized by an increase in serum creatinine or Blood Urea Nitrogen concentration. Due to the level of Blood Urea Nitrogen concentration returns to normal not long after it occurs, so that the benchmark for kidney damage therefore was marked by a decrease in urine production. Despite advances in the diagnosis

and staging of AKI with emergency biomarkers informing about the mechanisms and pathways of AKI, but mechanisms of AKI contributing to increased mortality and morbidity in hospitalized patients remains unclear. (Makris and Spanou, 2016) The development of early detection and AKI management has been improved through the development of universal definitions and staging spectrum. (Kellum *et al.*, 2012)

Due to logistical challenges and the danger of infection, a kidney biopsy is still only performed in a small minority of patients with COVID-19-associated AKI. Since most biopsies are only performed for diagnostic purposes, the true prevalence of abnormal alterations may still be unknown. As of now the majority of the information on the pathophysiology of COVID-19-related AKI comes from case reports and case series studies. (Sharma *et al.*, 2021) In the adult studies, most commonly encountered pathology are glomerular and tubular diseases such as Focal Segmental Glomerulosclerosis and Acute Tubular Injury (Santoriello *et al.*, 2020) There have been a research gap between the availability of the kidney biopsy between adult and children. (Sharma *et al.*, 2020) Although it should be noted that more than one compartment is more likely to be involved.

Therefore his research was proposed to study the alterations that occur in the kidney tissue due to Acute Kidney Injury in children diagnosed with COVID-19 to advance the knowledge pathology of the disease.

1.2. Research Problem

What are the histopathological findings of the kidney in pediatric patients with COVID-19 associated with Acute Kidney Injury?

1.3. Research Objective

General Objective

To identify the histopathological findings and clinical manifestations of Acute Kidney Injury in Pediatric COVID-19 patients

Specific Objective

To identify the most common histopathological findings of Acute Kidney Injury in Pediatric COVID-19 patients.

1.4. Benefits

1. To advance the knowledge of COVID-19 associated Acute Kidney Injury in Pediatric patients based from the histopathological findings of the kidney tissue.
2. To be used as precaution of the accompanying clinical manifestations in COVID-19 associated Acute Kidney Injury on Pediatric patients.