

**HISTOPATHOLOGICAL FINDINGS OF ACUTE KIDNEY INJURY IN
PEDIATRIC COVID-19 PATIENTS: A SYSTEMATIC REVIEW**



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Paper

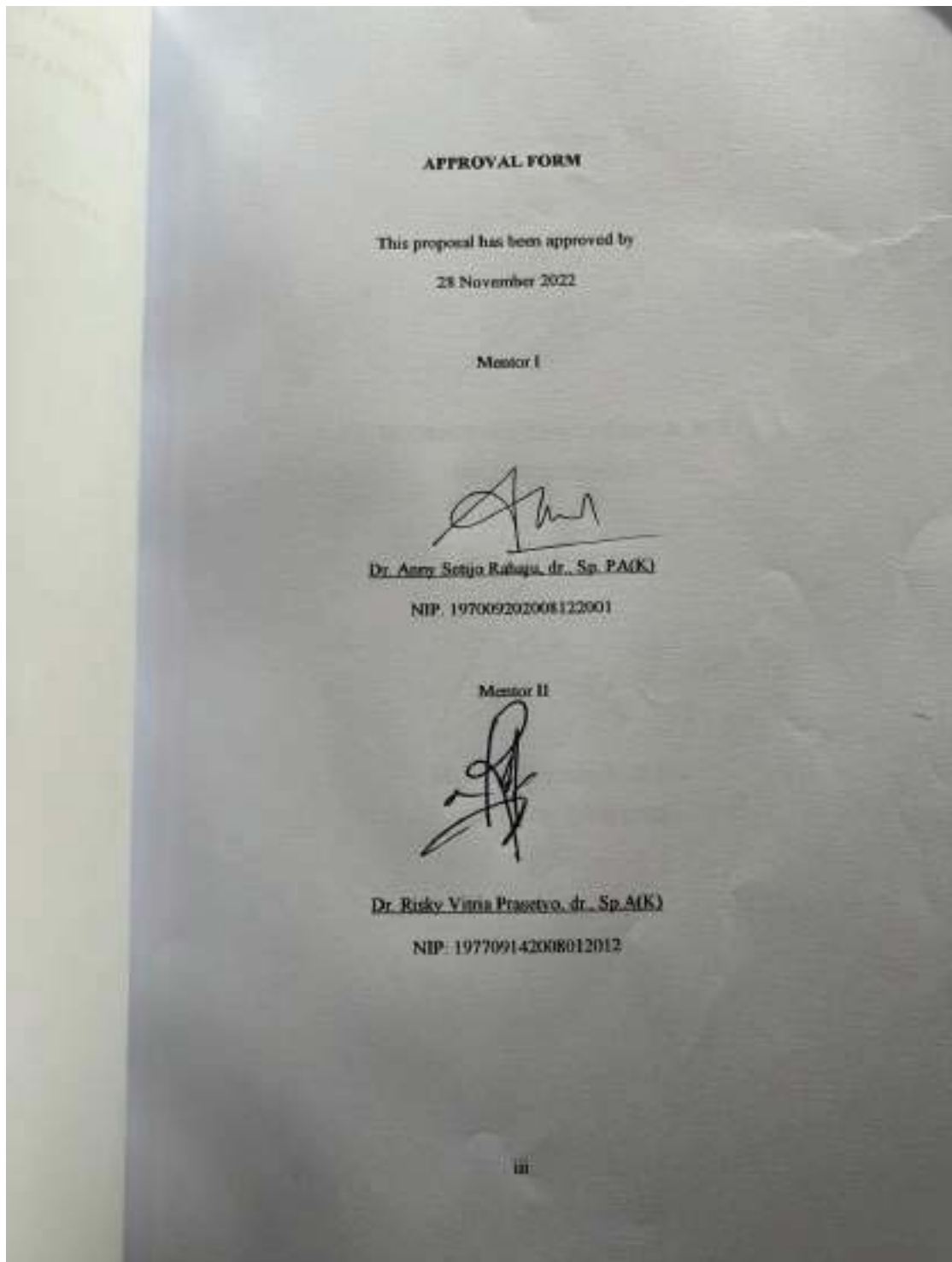
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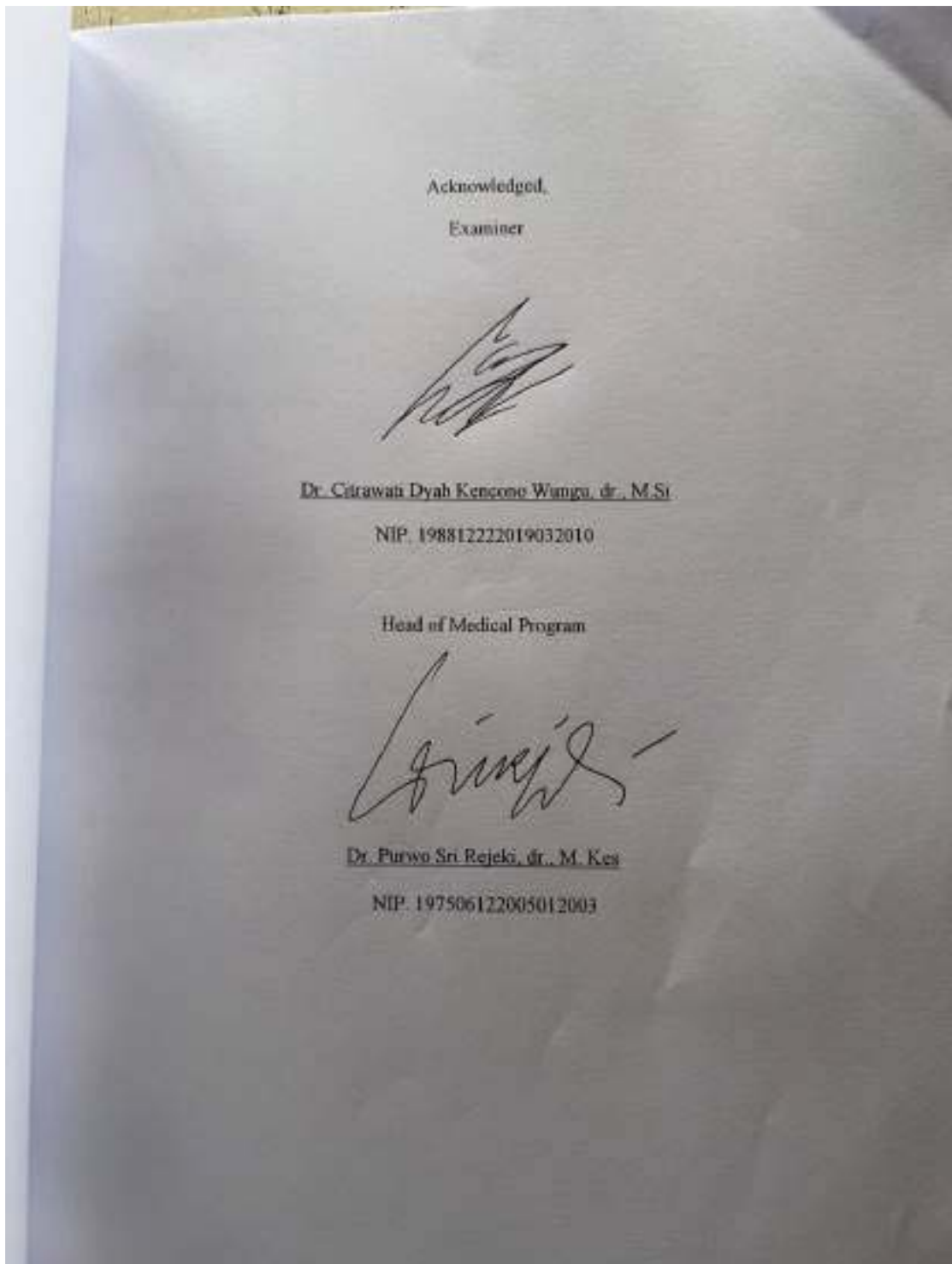
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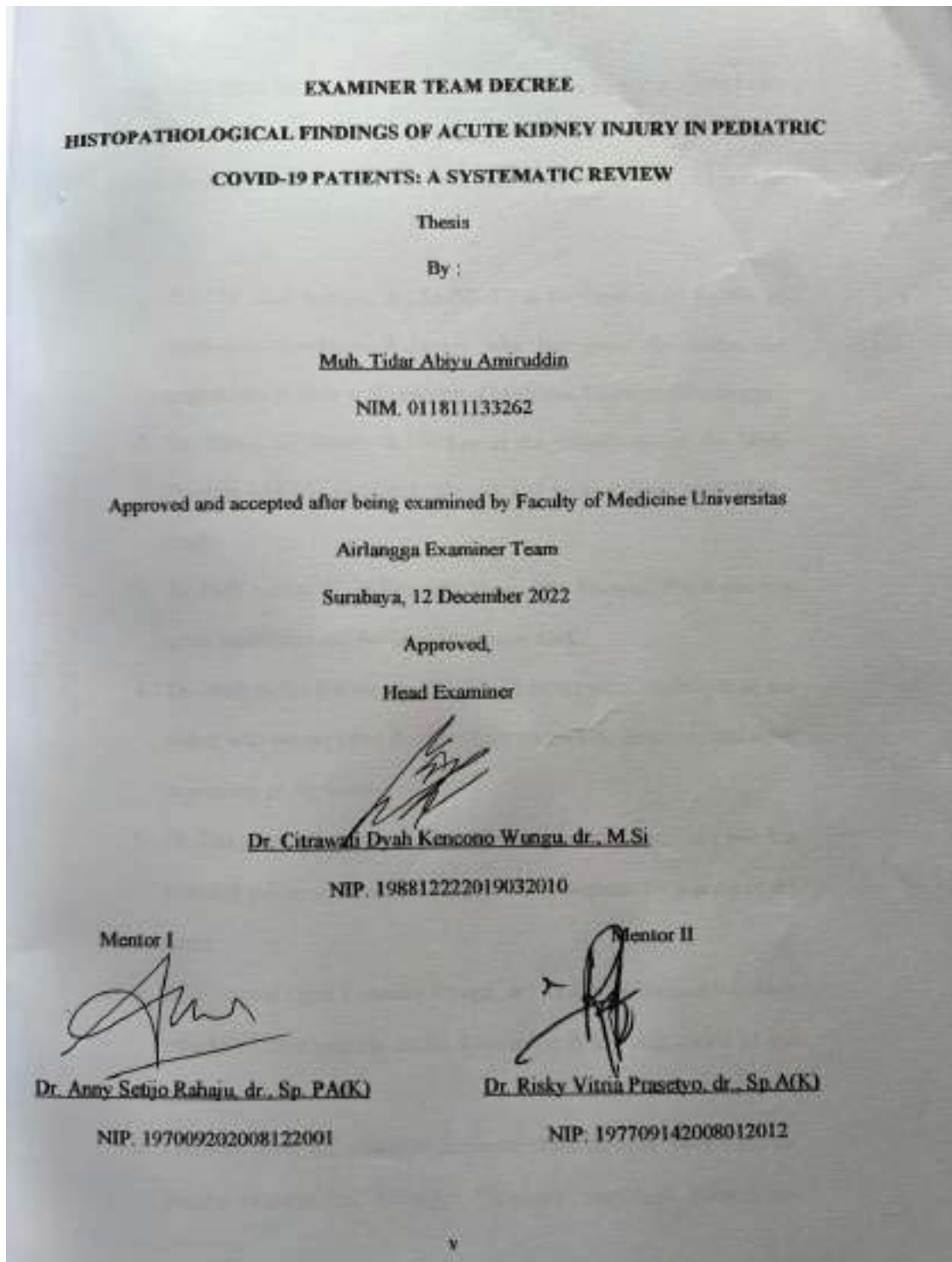
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ACKNOWLEDGEMENTS

Praise be to Allah SWT for all His grace and guidance so that the author can complete this thesis has been properly of course with the help from various parties. Therefore, on this occasion, I would like to express my deepest gratitude to:

1. Prof. Dr. Budi Santoso, dr., Sp. OG (K) as the Dean of the Faculty of Medicine, Universitas Airlangga who has given the author the opportunity to study at the Faculty of Medicine, Universitas Airlangga.
2. Dr. Purwo Sri Rejeki, dr., M.Kes as the Coordinator of the Study Program who has supported, allowed, and facilitated the work of the thesis.
3. Dr. Pudji Lestari, dr., M.Kes as the Head of the Research Block who has given permission and facilitated the thesis work.
4. Dr. Anny Setijo Rahaju, dr., Sp. PA(K) as the main supervisor of the author who always takes the time to guide, provide direction, and input in working on the thesis.
5. Dr. Risky Vitria Prasetyo, dr., Sp.A(K) as the second supervisor who has provided guidance, input, and suggestions throughout the making of the thesis.
6. Dr. Citrawati Dyah Kencono Wungu, dr., M.Sias the examiner lecturer who has helped provide useful knowledge in the preparation of this thesis.
7. Lecturers, staff, and education personnel of the Medical Study Program, Faculty of Medicine, Airlangga University, who have assisted and

provided lecture guidance to support the knowledge that became the basis for writing the thesis.

8. My parents, Prof. Dr. Muh. Dali Amiruddin Sp.KK(K) and Dyah Sri Sudarwati, for unconditionally providing the writer with love and encouragement.
9. My siblings, Dianawaty Amiruddin, Muh. Syakri Syahrir, Rina Previana, Muhammad Rum, Dyah Illiyen, and Isa Rifai who have always been the writer's source of critics and support.
10. My friends Julian, Naufal, Teddy, and especially Hafiza who have given relentless support, encouragement, and have been a great company for the writer.
11. Myself, who so far has been able to pick myself up and overcome the adversaries of life.
12. All parties involved in the completion of this thesis that cannot be mentioned one by one by the researcher.

The writer understands the need of improvement for the writing of this thesis, therefore positive suggestions and criticisms from the readers are much anticipated. With this thesis, the writer hopes that it can provide benefits for all parties in need.

Surabaya, 28 November 2022

Muh. Tidar Abiyu A.

SUMMARY

Coronavirus disease-19 (COVID-19) is a contagious infectious disease that is becoming a worldwide problem and has spread. COVID-19 has a very broad spectrum of symptoms with characteristics such as fever, sore throat, fatigue, cough, and shortness of breath. Acute kidney injury (AKI) is a complication of COVID-19 and the pathophysiology of AKI in COVID-19 could be determined as multi-factor. 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. The direct viral causes of AKI in COVID-19 are thought to be a direct viral injury, cytokine storm dysregulated inflammation, and vascular injury. However, other factors found in similar diseases have also been described, including hypovolemia, heart failure (right and left), sepsis, and dehydration. The exact prevalence of AKI in COVID-19 patients is growing over time as some study reports a low incidence rate of 0.5%; however, in a later study, the prevalence increased to 19%. 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. This research was proposed to study the alterations of kidney tissue along with the clinical manifestations and outcomes that occur of Acute Kidney Injury in children diagnosed with COVID-19.

This study was conducted using a Systematic Review adhering to PRISMA guidelines. The population of this study is pediatric patients that were infected with COVID-19 and later diagnosed with Acute Kidney Injury. Studies with no full access text available, written in languages other than English, and studies with only adult

patients were excluded from this study. Keywords used in this study were: “acute kidney injury” AND “histology” AND “children” OR “pediatric” AND “COVID”. Using those keywords, studies were systematically evaluated to obtain conclusions on the tissue alterations of the kidney and the clinical manifestation that occur of Acute Kidney Injury in children diagnosed with COVID-19.

The data extraction resulted in 7 studies in which 15 patients were included in the review. The review concluded that 88.8% (8/9) were Acute Tubular Necrosis, followed by 55.5% (5/9) both in Congestion and Thrombosis hence revealed the pathology as the main manifestation in pediatric AKI patients due to COVID-19. Further review should be done using meta-analysis when more studies have accumulated. More research is also needed to explore the pathology of kidney injury with more samples and detailed data such as the tissues samples slides, and laboratory results, all dated appropriately.

ABSTRACT

Introduction: Coronavirus disease-19 (COVID-19) is a contagious infectious disease that is becoming a worldwide problem and has spread. COVID-19 has a very broad spectrum of symptoms with characteristics such as fever, sore throat, fatigue, cough and shortness of breath. Acute Kidney Injury (AKI) is a complication of COVID-19 and the pathophysiology of AKI in COVID-19 could be determined as multi-factor. The exact prevalence of AKI in COVID-19 patients is growing over time. Similarly, the reported epidemiology of AKI in children infected with COVID-19 could vary. Due to the difficulties, kidney biopsy is performed in small minority of Acute Kidney Injury patients infected with COVID-19.

Objective: To identify the histopathological findings and clinical manifestations of Acute Kidney Injury in pediatric COVID-19 patients.

Methods: This study was conducted using a Systematic Review adhering to PRISMA guidelines. The population of this study is pediatric patients that were infected with COVID-19 as the intervention and later diagnosed with Acute Kidney Injury. Studies with no full access text available, written in languages other than English, and without histopathological data were excluded from this study. Keywords used in this study were: “acute kidney injury” AND “histology” AND “children” OR “pediatric” AND “COVID”. After obtaining eligible studies, the article is assessed with the Joanna Briggs Institute checklist for case report.

Result: The search yielded 279 studies. Next 45 duplicates were removed and then the remaining studies were screened through the title, abstract, and languages leaving 31 potential studies to be assessed. 24 studies were eliminated and 7 studies were selected as eligible. The clinical data shows the initial symptoms, each patient came to the hospital for different reasons but fever, abdominal pain, along with respiratory disturbances respectively are shown to be the common comorbid aligning with the pattern of the COVID-19 symptoms itself. In the histopathological report from the data, 88.8% (8/9) patients are found with acute tubular necrosis. The second commonly found pathological data from the histology report are congestion and thrombosis with both being present in 55.5% (5/9) patients each. Followed by Focal Segmental Glomerulosclerosis in 80% (4/5) patients. It should be noted that more than one pathology is found each patient.

Conclusion: The findings of the review indicate that Acute Tubular Necrosis, followed by Congestion and Thrombosis are the main histopathological manifestation in pediatric AKI patients due to COVID-19.

Keywords: *Histopathology, Acute Kidney Injury, COVID-19, pediatric.*

TABLE OF CONTENTS

APPROVAL FORM	iii
ACKNOWLEDGEMENTS	v
SUMMARY	ix
ABSTRACT	xi
TABLE OF CONTENTS	xii
LIST OF TABLES	xiv
LIST OF FIGURES	xv
ABBREVIATION	xvi
CHAPTER I	1
1.1 Background	1
1.2. Research Problem	3
1.3. Research Objective	4
General Objective	4
Specific Objective	4
1.4. Benefits.....	4
CHAPTER II.....	5
2.1 COVID-19.....	5
2.1.1 Definition	5
2.1.2 Pathophysiology.....	5
2.1.3 Etiology.....	7
2.1.4 Clinical Manifestations	7
2.1.5 Diagnosis.....	8
2.2 COVID-19 Associated Nephropathy	9
2.2.1 Epidemiology	11
2.2.2 Patophysiology.....	12
2.2.3 Histological Features	17
2.2.4 Asessment and Management.....	20
2.2.5 Outcome.....	22
CHAPTER III	23
3.1 Conceptual Framework.....	23
3.2 Conceptual Framework Explanation	24
CHAPTER IV	25
4.1 Types and Design of Research	25
4.1.1. Types of Research.....	25
4.1.2. Research Design.....	25

4.2. Population and Sample.....	25
4.2.1. Population	25
4.2.2. Study Sample	26
4.3. Research Variables and Operational Definition of Variables	26
4.4. Research Instruments.....	27
4.5. Location and Time of Research	27
4.5.1. Research Sites	27
4.6. Data Collection Procedure	27
4.7 Data collection and processing techniques	28
4.7.1 Data collection	28
4.7.2. Data Processing.....	28
CHAPTER V	31
CHAPTER VI	39
CHAPTER VII.....	43
7.1. Conclusion	43
7.2. Suggestion	43
REFERENCES.....	44

LIST OF TABLES

Table 2.1 pRIFLE Classification.....	11
Table 4. 1 PICO.....	25
Table 4. 2 Joanna Briggs Institute Checklist for Case Report Study.....	29
Table 5.1 Assessment using Joanna Briggs Institute Checklist.....	32
Table 5.2 Study Baseline Data	33
Table 5.3 Patient Demographic Data	35
Table 5.4 Histopathological Data.....	38

LIST OF FIGURES

Figure 2.2.4.1 Acute Tubular Injury in COVID-19 Kidney biopsy result	12
Figure 2.2.4.2 Glomerulus congestion and fibrin capillary thrombus.....	13
Figure 2.2.4.3 Fibrin thrombus in lumen of an artery.....	13
Figure 3.1 Conceptual Framework.....	16
Figure 5. 1 PRISMA Flowchart.....	22

ABBREVIATION

ACE2	: Angiotensin converting enzyme 2
AKI	: Acute kidney injury
ARDS	: Acute respiratory distress syndrome
ATI	: Acute tubular injury
ATN	: Acute tubular necrosis
CKD	: Chronic kidney disease
COVAN	: COVID-19 associated nephropathy
COVID-19	: Coronavirus disease 19
CSG	: Coronavirus study group
CT-Scan	: Computed tomography scan
ECMO	: Extracorporeal membrane oxygenation
FSGS	: Focal segmental glomerulosclerosis
GFR	: Glomerular filtration rate
LDH	: Lactate dehydrogenase
RT-PCR	: Reverse transcription – polymerase chain reaction
SARDS	: Severe acute respiratory distress syndrome
SARS-COV-2	: Severe acute respiratory syndrome due to COVID 19
SIRS	: Systemic inflammatory response system
WHO	: World health organization

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.