



بسم الله الرحمن الرحيم

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# **COVID 19 Related Multisystem Inflammatory Syndrome in Children Admitted to PICU in Ain Shams University Hospitals**

*Thesis*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قَالَ

لَسْبَّانِكَ لَا أَعْلَمُ لَنَا  
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

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# List of Abbreviations

Abb.	Full term
ACE2 .....	Angiotensin converting enzyme 2
ADE .....	Antibody dependant enhancement
AIDS .....	Acquired immunodeficiency syndrome
ANTI-S-IGG .....	Anti spike immunoglobulin G
ARDS .....	Acute respiratory distress syndrome
BMI .....	Body mass index
CAA .....	Coronary artery aneurysm
CNS .....	Central nervous system
CORAD .....	CT signs were analyzed quantitatively using a radiologic scoring system
CRP .....	C-reactive protein
ECMO .....	Extra corporeal membrane oxygenation
ESR .....	Erythrocyte sedimentation rate
FDA .....	Food and Drug administration
GCSF .....	Granulocyte-colony stimulating factor
GIT .....	Gastrointestinal tract
H1N1 .....	Hemagglutinin type 1 and Neuraminidase type 1
HCoV .....	human coronavirus
HIV .....	Human immunodeficiency virus
HLH .....	Hemophagocytic lymphohistiocytosis
IFN .....	Interferon
IL .....	Interleukin
IL1 .....	Interleukin 1
IL10 .....	Interleukin 10
IL6 .....	Interleukin 6
INF .....	Interferon
IP10 .....	Human interferon-inducible protein 10
IVIG .....	Intravenous immune globulin
KD .....	Kawasaki Disease
KDSS .....	Kawasaki Disease Shock Syndrome
LDH .....	Lactate dehydrogenase.
MAS .....	Macrophage activation syndrome

# List of Abbreviations *cont...*

Abb.	Full term
MCP1	Monocyte chemotactic protein-1
MERS-CoV	Middle Eastern respiratory syndrome coronavirus
MIP1A	Macrophage inflammatory protein 1 a
MIS-C	Multisystem inflammatory syndrome in children
PARDS	Pediatric Acute Respiratory Distress Syndrome.
PICU	Pediatric intensive care unit
RAS	Renin-angiotensin system
RR	Respiratory rate
RT-PCR	Reverse transcriptase-polymerase chain reaction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus
SARS-HCoV	Severe Acute Respiratory Syndrome human coronavirus
SHLH	Secondary hemophagocytic lymphohistiocytosis
SPO2	Oxygen saturation
ssRNA	Positive-sense single-stranded RNA
TNF	Tumor necrosis factor
TNF- $\beta$	Tumor necrosis factor $\beta$
TSS	Toxic shock syndrome
TSS	Toxic shock syndrome
VIS	Vasoactive-inotropic score

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# INTRODUCTION

Severe acute respiratory syndrome coronavirus (SARS-CoV-2) infection has rapidly spread worldwide since it was first identified in China in late 2019, with subsequent epicenters being recognized in Europe and the U.S. Previous reports of SARS-CoV-2 infection indicated that young children were disproportionately spared from infection (*CDC, 2020; Parri et al., 2020*).

Although it remains unclear if this is due to a lack of detection because of predominantly asymptomatic or mild disease in this age group. In the latter half of April 2020, a novel syndrome in children and adolescents termed “multisystem inflammatory syndrome in children” (MIS-C) with likely relation to SARS-CoV-2 infection was first described. Initial reports surfaced in the UK (*Riphagen et al., 2020*) and Italy (*Verdoni et al., 2020*), followed by New York and other parts of the U.S. Preliminary accounts of the features of this syndrome resemble those of known entities such as Kawasaki Disease (KD), toxic shock syndrome (TSS), and secondary hemophagocytic lymphohistiocytosis (SHLH)/macrophage activation syndrome (MAS).

## **AIM OF THE WORK**

To evaluate the clinical profiles, risk factors, and outcome for pediatric multisystem inflammatory syndrome in children with COVID-19 admitted to PICU.

# COVID 19

## Classification and origin:

SARS-CoV-2 is a member of the family Coronaviridae and order Nidovirales. The family consists of two subfamilies, Coronavirinae and Torovirinae and members of the subfamily Coronavirinae are subdivided into four genera: (a) Alphacoronavirus contains the human coronavirus (HCoV)-229E and HCoV-NL63; (b) Betacoronavirus includes HCoV-OC43, Severe Acute Respiratory Syndrome human coronavirus (SARS-HCoV), HCoV-HKU1, and Middle Eastern respiratory syndrome coronavirus (MERS-CoV); (c) Gammacoronavirus includes viruses of whales and birds and; (d) Deltacoronavirus includes viruses isolated from pigs and birds (*Burrell et al., 2016*).

SARS-CoV-2 belongs to Betacoronavirus together with two highly pathogenic viruses, SARS-CoV and MERS-CoV. SARS-CoV-2 is an enveloped and positive-sense single-stranded RNA (+ssRNA) virus (*Kramer et al., 2006*).

SARS-CoV-2 is considered a novel human-infecting Betacoronavirus (*Lu et al., 2020*). Phylogenetic analysis of the SARS-CoV-2 genome indicates that the virus is closely related (with 88% identity) to two bat-derived SARS-like coronaviruses collected in 2018 in eastern China (bat-SL-CoVZC45 and bat-SL CoVZXC21) and genetically distinct

from SARS-CoV (with about 79% similarity) and MERS-CoV (*Lu et al., 2020*).

### **Routes of Transmission:**

Currently, respiratory droplets and contact transmission are considered to be the main transmission routes. Other reports indicate that SARS-CoV-2 can be detected in the urine and stool of laboratory confirmed patients, implying a risk of fecal–oral transmission (*General Once of National Health Commission, 2020*).

### **The incubation period:**

It has been found to be as long as 19 or 24 days (*Huang et al., 2020; Chu et al., 2020*), although case definitions typically rely on a 14 day window (*World Health Organization, 2020*). The basic reproductive number (R0) has been estimated with varying results and interpretations. R0 measures the average number of infections that could result from one infected individual in a fully susceptible population (*Bauch & Oraby, 2013*). Studies from previous outbreaks found R0 to be 2.7 for SARS (*Riley et al., 2003*) and 2.4 for 2009 pandemic H1N1 influenza (*Yang et al., 2009*). One study estimated that that basic reproductive number (R0) was 2.2 (95% CI: 1.4–3.9) (*Li et al., 2020*). However, later in a further analysis of 12 available studies found that R0 was 3.28 (*Liu et al., 2020*).