بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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MONA MAGHRABY

Interferon- gamma-induced protein-10 (IP-10)/ CXCL10 Serum Level and Natural Killer Cell Count as Predictive Factors for the Severity of COVID-19

Thesis

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Mai Mustafa Mounir Yasin

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List of Abbreviations

Abb.	Full term

ACE2 ..... *Angiotensinconverting enzyme 2*

ADE ..... *Antibody-Dependent Enhancement*

ALI..... *Acute lung injury*

ALT..... *Alanine aminotransferase*

AP-1..... *Activating protein*

APCs..... *Antigen presentation cells*

ARDS..... *Acute respiratory distress syndrome*

AST..... *Aspartate aminotransferase*

BAL..... *Bronchoalveolar lavage*

BALF..... *Broncho-alveolar lavage fluid*

CoV..... *coronavirus*

COVID-19..... *Coronavirus disease 2019*

CRP..... *C-reactive protein*

CSF..... *Colony-stimulating factors*

CT..... *computed tomography*

CXR ..... *Chest X-ray*

DAD..... *Diffuse alveolar damage*

DCs ..... *Dendritic cells*

ELISA..... *Enzyme -linked immuno sorbent assay*

HFNC ..... *High flow nasal cannula*

HRV-16..... *Human rhinovirus type 16*

ICU ..... *Intensive care unit*

IFN ..... *Interferon*

List of Abbreviations (Cont…)

Abb.	Full term
IL	*Interleukin*
IP-10	*Interferon γ-induced protein 10*
IRF	*Interferon regulatory factor*
IRF9	*Interferon regulatory factor 9*
ISGF3	*Interferon-stimulated gene factor 3*
ISREs	*IFN-stimulated response elements*
JAK-STAT	*Janus kinase–signal transducer and activator of transcription*
KIRs	*Killer Immunoglobulin-like Receptors*
LAV	*Live-attenuated vaccine*
mAb	*Monoclonal antibody*
MCP1	*Monocyte chemoattractant protein*
MDA5	*Melanoma differentiation-associated gene 5*
mDC	*Myeloid DCs*
MERS-CoV	*Middle East Respiratory Syndrome*
MHC	*Major histocompatibility complex*
MIG	*Monokine induced by IFN-γ*
moDC	*Monocyte derived dendritic cells*
NCRs	*Natural Cytotoxicity Receptors*
NHC	*National Health Commission of the People's Republic of China*
NK	*Natural killer*
nsps	*Non- structural proteins*
PAMPs	*Pathogen Associated Molecular Patterns*

List of Abbreviations (Cont…)

Abb.	Full term
PBMCs	*Peripheral blood mononuclear cells*
PD1	*Programmed cell death protein 1*
pDC	*Plasmacytoid DCs*
PE	*Pulmonary embolism*
PRR	*Pattern Recognition Receptors*
RBD	*Receptor binding domain*
RIG-I	*Retinoic acid-inducible gene I*
RLRs	*RIG-I-like receptors*
rRT-PCR	*Real-time reverse transcription polymerase chain reaction*
RTC	*Replicase transcriptase complex*
SARS-CoV	*Severe Acute Respiratory Syndrome*
SARS-CoV-2	*Severe Acute Respiratory Syndrome Coronavirus 2*
TGFβ	*Transforming growth factor β*
TH	*T helper cell*
TLC	*Total leucocytic count*
TLRs	*Toll-like receptors*
TNFα	*TUMOR necrosis factor α*
WHO	*World health organization*

INTRODUCTION

Coronavirus is a common pathogen that mostly affects the respiratory system of humans. The Severe Acute Respiratory Syndrome (SARS-CoV) and the Middle East Respiratory Syndrome (MERS-CoV) are two previous coronavirus (CoV) outbreaks ***(Rothan & Byrareddy, 2020).*** Recently, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has resulted in the major global pandemic of COVID 19.

COVID 19 disease symptoms range from mild to severe, and critically ill individuals are more likely to develop acute respiratory distress syndrome (ARDS) and multiorgan damage. It rapidly became a critical target of research to determine predictors of severity to guide therapeutic intervention.

Increased serum levels of proinflammatory cytokines have been linked to pulmonary inflammation and significant lung damage in COVID-19 patients ***(Qin et al., 2020).***

Initially in The immune response to viral infections, the infected cells produce type I interferons, which have an antiviral impact and activate cells like natural killer (NK) cells ***(Masselli et al., 2020)***. NK cells, which are well-known for their major role in combating viral infections, kill virally infected cells and release cytokines including IFN-γ, which activate other cells. Natural killer cells (NK cells) are innate

immune responders that play a key role in virus clearance and immunomodulation. Despite their importance in viral infection, the role of natural killer cells in combatting SARS-CoV-2 has not yet been directly studied ***(Market et al., 2020).***

A surge of proinflammatory cytokines and chemokines is detected following NK and T cell activation. These cytokines activate the adaptive immune response and attract additional immune cells to the infection site. The release of increased amounts of pro-inflammatory cytokines, including IFN-γ, IL-1β, IL-6, IL-12, IL-18, IL-33, TGFβ, TNFα and chemokines including IP-10, CXCL8, CXCL9, CCL5, CCL2, CCL3, trigger and prolong the uncontrolled systemic inflammatory response ***(Coperchini et al., 2020).***

More recently, interest has been shown in the chemokine interferon γ-induced protein 10 kDa (IP-10) /CXCL10, which belongs to the CXC chemokine family. It is secreted from leukocytes, stromal cell, epithelial cells and endothelial cells in response to IFN-γ. It binds to the receptor CXCR3, which is found mostly on activated T lymphocytes and natural killer cells. IP-10 induces chemotaxis, apoptosis and cell growth inhibition. Abnormal levels of IP-10 have been found in the body fluids of individuals infected with some viruses ***(Liu et al., 2011)***. Human airway epithelial cells have been found to release IP-10 in response to human rhinovirus type 16 (HRV-16). This IP-10 contribute to lymphocyte recruitment to the airways, and disease severity in asthma and chronic obstructive pulmonary disease