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بسم اللّه الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات

قسم التوثيق الإلكتروني

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم باللّه العظيم أن المادة التي تم توثيقها وتسجيلها

علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

Ain-Shams University
Faculty of Medicine
Internal medicine and nephrology

The Assessment of Immunological Status in Hemodialysis Patients Post COVID-19 Infection

Thesis
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In Internal medicine

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قُلْ إِنَّ صَلاَتِي وَنُسُكِي وَمَحْيَايَ
وَمَمَاتِي لِلّهِ رَبِّ الْعَالَمِينَ *
لاَ شَرِيكَ لَهُ وَبِذَلِكَ أُمِرْتُ وَأَنَاْ
أَوَّلُ الْمُسْلِمِينَ

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Enas Fathe Hassan Elkholy

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List of abbreviations

ACE-2	angiotensin converting enzyme 2
ADCC	antibody-dependent cellular cytotoxicity
ADE	antibody-dependent enhancement
ALI	acute lung injury
ARBs	angiotensin receptor blockers
ARDS	acute respiratory distress syndrome
CDC	Centers of disease control
CKD	chronic kidney disease
CLpro	chymotrypsin-like protease
COPD	chronic obstructive pulmonary disease
COVID-19	Coronavirus disease 2019
CRP	C-reactive protein
CRS	cytokine release syndrome
CVD	cardiovascular disease
ELISA	enzyme linked immunosorbent assays
FcγRIIIa	Fc-receptor
HD	hemodialysis
ICTV	International Committee on Taxonomy of Viruses
ICUs	intensive care units
IFA	immunofluorescence assays
IgG	immunoglobulin G
IL	Interleukin
LAG-3	lymphocyte-activation gene-3
MASP-2	mannan-binding lectin-associated serine protease 2
MDs	Metabolic disorders
MERS-CoV	Middle East respiratory syndrome coronavirus
MHC-I	major histocompatibility complex class I
Mpro	main protease
NAT	nucleic acid tests
NK	natural killer
NKG2A	NK group 2 member A
NLRP3	nucleotide-binding domain and leucinerich repeat pyrin domain 3
nsps	non-structural proteins
ORF8	open reading frame 8
ORFs	open reading frames
PAMPs	pathogen-associated molecular patterns
PD-1	death protein 1

PPE	personal protective equipment
RAS	renin–angiotensin system
RBD	receptor binding domain
RCT	replication-transcription complex
RT-PCR	Reverse transcription polymerase chain reaction
SARS	severe acute respiratory syndrome
SARS-CoV	severe acute respiratory syndrome coronavirus
sgRNAs	subgenomic RNAs
TH1	T helper 1
TIM-3	T-cell immunoglobulin
TLRs	toll-like receptors
WHO	World health organization

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Introduction

Coronavirus disease 2019 (COVID-19) is an outbreak due to SARS-CoV-2, a new virus of Coronaviridae family, emerged in China in December 2019 and declared by the World Health Organization a global pandemic on March 2020.

Hemodialysis patients have impaired immune function, so they constitute a group at risk of suffering covid-19 infection and possibly with a high incidence of complications. Furthermore, they visit a medical center regularly (3 times per week), with more than 4 hours per day, they are at high risk more than general population(**G. Grasselli** ,et al. 2020)

Thus, it can be stated that a Dialysis unit is a place that deserve special consideration in relation with the epidemiology of Covid -19. Several diagnostic strategies are available to identify current infection, rule out infection and test for past infection and immune response.

The immune system produces proteins called antibodies in response to SARS-CoV-2, the virus that causes COVID-19. The researchers found that levels of an antibody called immunoglobulin G (IgG) remained elevated in infected patients However, due to the recent emergence of SARS-CoV-2 in the human population, it is not known how long antibody responses will be maintained or whether they will provide protection from reinfection.

Antibody testing to covid_19 by Enzyme-Linked Immuno-Sorbent Assay (ELISA) is highly sensitive and specific and may indicate prior infection. Antibody responses to SARSCoV-2 can be detected in most infected individuals 10–14 d after the onset of COVID-19

symptoms.Serological tests detect antibodies against spike protein (S) and/or nucleoprotein (N) since these are the most immunogenic proteins of SARS-CoV-2 (Morawska L,et al.2020).

The S protein, consisting of a S2 and a S1 subunit with a receptor binding domain (RBD), is present on the envelope and is used by the virus to connect to the human cells using the ACE-2 receptor. Since antispike protein antibodies have been shown to possess neutralizing effects in vitro, it has been suggested that detection of antibodies against spike protein could provide a better indication of an effective immune response**(Korber B ,et al.2020.)**

It was important to figure these changes out in this study and to investigate the difference of immune responses

Aim of The Work

Detection of the level of immunoglobulin (IgG) antibodies against covid _19 virus to assess the immunological status of the patients post covid_19 infection and the risk of reinfection with covid _19.

Chapter (1)

COVID-19

Coronaviruses belong to the Coronaviridae family in the Nidovirales order. Corona represents crown-like spikes on the outer surface of the virus; thus, it was named as a coronavirus. Coronaviruses are minute in size (65–125 nm in diameter) and contain a single-stranded RNA as a nucleic material, size ranging from 26 to 32kbs in length (Fig. 1). The subgroups of coronaviruses family are alpha (a), beta (b), gamma (c) and delta (d) coronavirus**. (Di Gennaro et al., 2020).**

The severe acute respiratory syndrome coronavirus (SARS-CoV), H5N1 influenza A, H1N1 2009 and Middle East respiratory syndrome coronavirus (MERS-CoV) cause acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) which leads to pulmonary failure and result in fatality. These viruses were thought to infect only animals until the world witnessed a severe acute respiratory syndrome (SARS) outbreak caused by SARS-CoV, 2002 in Guangdong, China **(Khatib et al., 2020).** Only a decade later, another pathogenic coronavirus, known as Middle East respiratory syndrome coronavirus (MERS-CoV) caused an endemic in Middle Eastern countries**(N. Wang et al., 2013).**

At the end of 2019, Wuhan an emerging business hub of China experienced an outbreak of a novel coronavirus that killed more than eighteen hundred and infected over seventy thousand individuals within the first fifty days of the epidemic. This virus was reported to be a member of the b group of coronaviruses. The novel virus was named as Wuhan coronavirus or 2019 novel coronavirus (2019-nCov) by the Chinese researchers.

The International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2 and the disease as COVID-19 **(Cui et al., 2019),(Organization, 2020a).** In the history, SRAS-CoV (2003) infected 8098 individuals with mortality rate of 9%, across 26 countries in the world, on the other hand, novel corona virus (2019) infected 120,000 individuals with mortality rate of 2.9%, across 109 countries, till date of this writing. It shows that the transmission rate of SARS-CoV-2 is higher than SRAS-CoV and the reason could be genetic recombination event at S protein in the RBD region of SARS-CoV-2 may have enhanced its transmission ability.

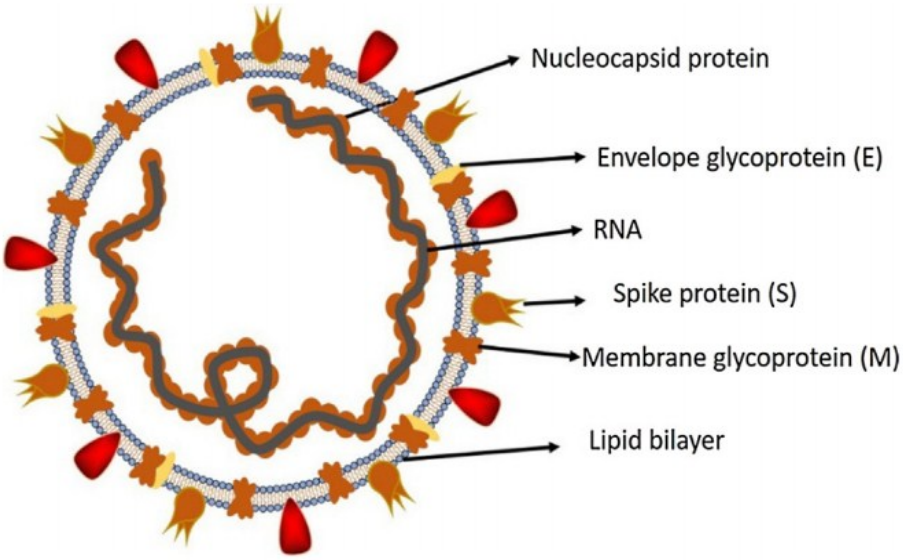

Fig. 1: Structure of respiratory syndrome causing human coronavirus **(John et al., 2015)**

Epidemiology

The COVID-19 epidemic expanded in early December from Wuhan, China's 7th most populous city, throughout China and was then exported to a growing number of countries. The first confirmed case of