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Complications after SARS-2/COVID-19 Viral Infection in Recovered Patients: Prospective follow up Study.

A Research submitted to the college of pharmacy university of Babylon as partial fulfillment of the requirement for bachelor's degree in pharmacy

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بسم الله الرحمن الرحيم

﴿فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَى إِلَيْكَ وَحْيُهُ وَقُلْ رَبِّ زِدْنِي عِلْمًا﴾

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صدق الله العلي العظيم

Dedication

We dedicated this search to the Almighty God, thank you for the guidance, strength, power of mind, protection and skills and for giving us a healthy life. All of these, we offer to you

This study is also wholeheartedly dedicated to our beloved parents, who have been our source of inspiration and gave us strength when we thought of giving up, who continually provide their moral, spiritual, emotional, and financial support.

To our brothers, sisters, relatives, mentor, friends, and classmates who shared their words of advice and encouragement to finish this study.

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Abstract

The current COVID-19 pandemic is caused by a coronavirus named SARS-CoV-2 which cause respiratory diseases in humans, from the common cold to infrequent and serious diseases. The first human cases of COVID-19 were reported from Wuhan City, China, in December 2019. The entry mechanism of a coronavirus depends upon cellular proteases that include, human airway trypsin-like protease (HAT), cathepsins and transmembrane protease serine 2 (TMPRSS2) which split the spike protein and reside further penetration changes. Angiotensin-converting enzyme 2 (ACE2) is a key receptor for SARS-coronavirus. The most common symptoms of COVID-19 are fever, dry cough and fatigue. According to present evidence, COVID-19 virus is primarily transmitted between people over respiratory droplets and contact routes. Approximately, as of 15 May 2022, 521 million and 347 thousand person infected with covid-19 over the world while 6 million and 250 thousand persons dead with covid-19 over the world. We conducted a prospective study of 200 Iraqi recovered patients with a spectrum of post COVID-19. A google form questionnaire symptoms and complications followed up from recovery until these days was performed

to collect a required data that included gender of the patients, age, family history, genetic diseases, presence of chronic disease, date of infection, symptoms and complications other additional information and after SARS-2/COVID-19 viral infection in recovered patients. Out of a total of 200 patients were 127 (63.5%) women and 73(36.5%) men. Only 9% of all subjects have no manifestation after recovery from the disease while a large percentage of subjects suffered from several symptoms and diseases. As reported of 37 years' male had manifested with impotence due to COVID-19 infection could affect male sexual function through endothelial damage in erectile tissue, testicular damage, and psychological alterations. People who have recovered from COVID-19 should be more careful in maintaining and monitoring their health status. They have to be in regular monitoring for their future complications that may occur after their recovery. Those recovered patients are recommended to get CT, and Magnetic resonance imaging (MRI) scans and University of Pennsylvania Smell Identification Test (UPSIT) to test smell identification, as loss of smell is one of the initial symptoms of neuroinvasion in COVID-19 patients.

Aim of research

This research was done to detect the repercussions of SARS-2\covid-19 and complications after recovery which covid-19 can cause it to the infected patient. Also to find out more about the behavior of the virus from a scientific point of view.

1. Introduction.

The current COVID-19 pandemic is caused by a coronavirus named SARS-CoV-2 which is single-stranded RNA, enveloped virus. The first human cases of COVID-19 were reported from Wuhan City, China, in December 2019. Coronaviruses (CoVs) are a huge family of viruses, many of which cause respiratory diseases in humans, from the common cold to infrequent and serious diseases such as the Severe Acute Respiratory Syndrome

(SARS) and the Middle East respiratory syndrome (MERS), both of which have high mortality rates and were determined for the first time in 2003 and 2012, respectively. CoVs have four genera: alpha-, beta-, gamma- and delta-CoV. All CoVs presently known to cause disease in humans belong to the alpha- or the beta-CoV. Many of these CoVs can infect numerous animal species as well [1].

The SARS-COV-2 can be diagnostic in different methods such as laboratory methods (such as CT-scan, chest X-ray, clinical history of patients, high level of cytokine IL2, IL4, IL6, IL7, IL10) The quantitative Reverse-Transcription Polymerase Chain Reaction (RT-PCR), Enzyme Immunoassay (EIA) or Enzyme-Linked Immunosorbent Assay (ELISA), Immunochromatographic tests (rapid tests) and Microarray [2].

Many reports from diverse parts of the world have shown that COVID-19 has a set of long-term effects on almost all systems including respiratory, cardiovascular, gastrointestinal, neurological, psychiatric, and dermatological systems. A considerable part of patients, up to 87%%, recovering from acute infection continue to experience from a set of symptoms including dyspnea, cough, myalgia, fatigue, and headache. The data that people who have mild illness or no symptoms during acute infection also suffer from long-term symptoms exhibit that the disease causes greater damage than appears in infected persons [3].

1.1 Mechanism of infection.

All coronaviruses contain specific genes in ORF1 regions that encode proteins for viral replication, nucleocapsid and spikes formation. The attachment and entry of the virus to the host cells occur due to glycoprotein spikes that located in the outer surface of coronavirus. The entry mechanism of a coronavirus depends upon cellular proteases that include, human airway trypsin-like protease (HAT), cathepsins and transmembrane protease serine 2 (TMPRSS2) which split the spike protein and reside further penetration changes. Angiotensin-converting enzyme 2 (ACE2) is a key receptor for SARS-coronavirus [4].

SARS-CoV-2 retain the typical coronavirus structure with spike protein and also expressed other polyproteins, nucleoproteins, and membrane proteins, such as RNA polymerase, 3-chymotrypsin-like protease, papain-like protease, helicase, glycoprotein, and accessory proteins. The spike protein of SARS-CoV-2 contains a 3-D structure in the RBD region to maintain the van der Waals forces. The 394 glutamine residue in the RBD region of SARS -CoV-2 is recognized by the critical lysine 31 residue on the human ACE2 receptor [4]. The entire mechanism of pathogenicity of SARS-CoV-2, from attachment to replication is well mentioned in figure. 1.

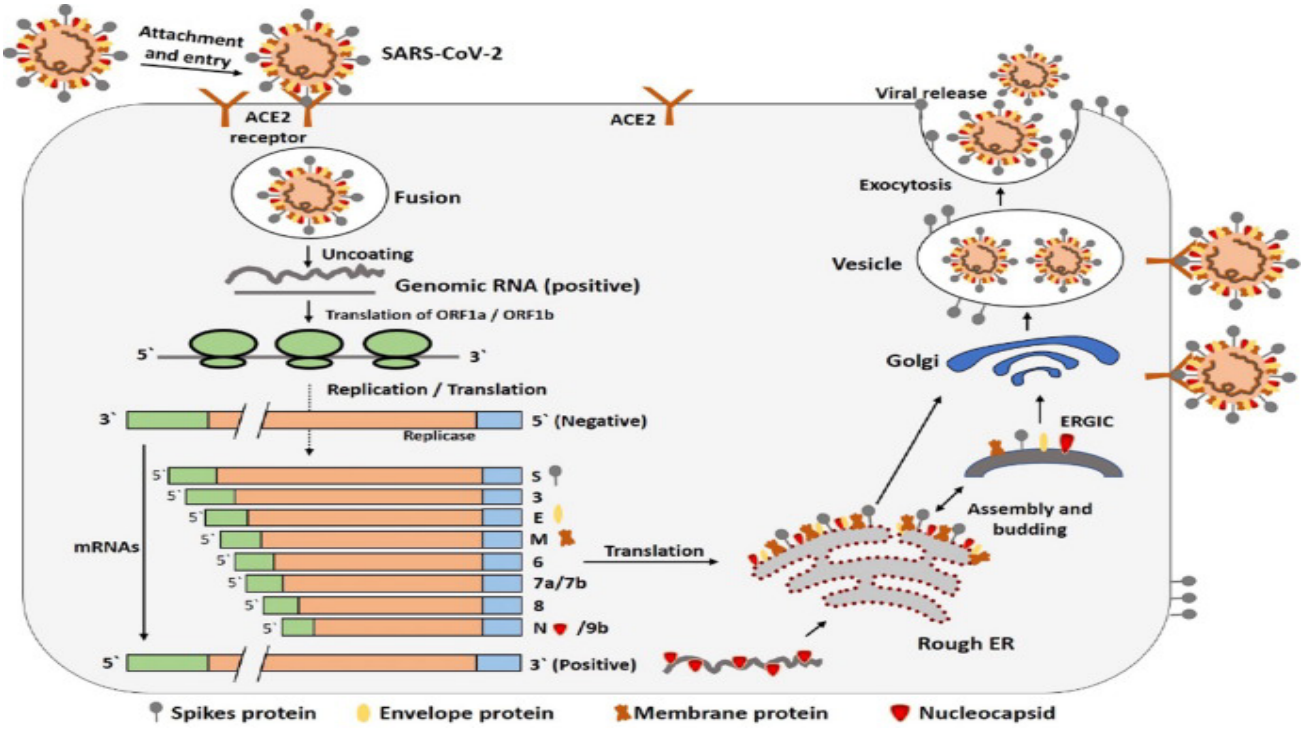

Figure 1. The life cycle of SARS-CoV-2 in host cells; its life cycle begins when S protein binds to the cellular receptor ACE2. After receptor binding, the conformation change in the S protein facilitates viral envelope fusion with the cell membrane through the endosomal pathway. Then SARS-CoV-2 releases RNA into the host cell. Genome RNA is translated into viral replicas polyproteins pp1a and 1ab, which are then cleaved into small products by viral proteinases. The polymerase produces a series of sub genomic mRNAs by discontinuous transcription and finally translated into relevant viral proteins. Viral proteins and genome RNA are subsequently assembled into virions in the ER and Golgi and then transported via vesicles and released out of the cell. ACE2, angiotensin-converting enzyme 2; ER, endoplasmic reticulum; ERGIC, ER–Golgi intermediate compartment [4].

1.2 Symptoms of COVID-19.

The most common symptoms of COVID-19 are fever, dry cough and fatigue. These symptoms can also see in other caused diseases such as influenza, common cold and other respiratory caused disease. Other symptoms which are less common and may affect some patients include, loss of taste or smell, nasal congestion, conjunctivitis, sore throat, headache, muscle or joint pain, different types of skin rash, nausea or vomiting, diarrhea, chills or dizziness. While symptoms of severe COVID-19 disease may include: shortness of breath, loss of appetite, confusion, persistent pain or pressure in the chest and high temperature (above 38 °C). Other less common symptoms are: irritability, reduced consciousness, anxiety, depression, sleep disorders.

More severe and infrequent neurological complications such as strokes, brain inflammation, delirium and nerve damage. [5]

1.3 Modes of transmission of the COVID-19 virus.

Respiratory infections can be transmitted over droplets of different sizes (when the droplet particles are >5-10 μm in diameter they are referred to as respiratory droplets, and when then are <5μm in diameter, they are referred to as droplet nuclei). According to present evidence, COVID-19 virus is primarily transmitted between people over respiratory droplets and contact routes.

Transmission of droplet occurs when a person is in close contact (within 1 m) with someone who has respiratory symptoms (e.g., coughing or sneezing) and is then at risk of having their mucosae (mouth and nose) or conjunctiva (eyes) exposed to potentially infective respiratory droplets. Transmission may also take place through fomites in the existing environment around the infected person. Therefore, transmission of the COVID-19 virus can take place by direct contact with infected people and indirect contact with surfaces in the existing environment or with contraption used on the infected person (e.g., stethoscope or thermometer).

Transmission of airborne is different from transmission of droplet as it refers to the presence of microbes inside droplet nuclei that are generally

considered to be particles <5μm in diameter, can exist in the air for long periods of time and can be transmitted to other people over distances greater than 1 m.

In the condition of COVID-19, transmission of airborne may be potential in specific circumstances and settings in which procedures or support treatments which generate aerosols are performed; i.e., endotracheal intubation, bronchoscopy, open suctioning, administration of nebulized treatment, manual ventilation before intubation, turning the patient to the prone position, disconnecting the patient from the ventilator, non-invasive positive-pressure ventilation, tracheostomy, and cardiopulmonary resuscitation.

There is some evidence that infection of COVID-19 may lead to intestinal infection and be present in faeces. Yet, to date only one study has cultured the COVID-19 virus from a single stool specimen. There have been no reports of faecal–oral transmission of the COVID-19 virus to date. [6]

1.4 Number of infected people with covid-19 over world.

Approximately, as of 15 May 2022, 521 million and 347 thousand persons was infected with covid-19 over the world while 6 million and 250 thousand persons dead with covid-19 over the world. This table presents the top five countries in terms of number of people infected and dead with covid-19. [7]

Country	*Cases*	*deaths*
United state	82.4 M	998K
India	43.1 M +2,202	524K +27
Brazil	30.7 M +6,296	665K +46
France	28.4 M +22,844	144K +7
Germany	25.7 M +2,305	137K

Table1: the top five countries in term of number of people infected and dead with covid-19. (M: million, K: thousand.)

In Iraq, as of 15 May 2022, the number of people was infected with covid-19 is 2 million and 326 thousand and 458 while the people dead was 25 thousand and 216. [7]

1.5 Literature review.

- [Bircan Kayaaslan et al,2021]: *they* performed a special questionnaire to check about the presence of persistent symptoms beyond 12 weeks from the first diagnosis. Their prospective study was conducted in patients with COVID-19 who were hospitalized in COVID-19 wards or followed in outpatient clinics in Ankara City Hospital, between August 1, 2020, and October 31, 2020. In their study, they assessed the prevalence and characteristics of the post-COVID syndrome in a considerable population consisted of 1007 patients recovered from acute COVID-19 and demonstrated that half of the patients suffer from persistent symptoms, although more than 4 months have passed after acute infection. Their results showed that a plentiful part of patients with COVID-19 had persistent symptoms even 4–5 months after COVID-19 diagnosis, and even patients with a mild-to-moderate disease suffered from persistent symptoms. Although the persistent symptoms of the patients are not vital, follow-up of these symptoms in the post recovery period is important due to its resulting disrupting life quality. [8]

- [Francesca Salamanna et al,2021]; Their search was carried out on PubMed, Web of Science, EMBASE, and Google Scholar databases to identify all type of papers on the long-term symptoms of COVID-19 in Italy. Their study review allowed them to outline that a noteworthy number of patients present long-lasting *sequelae*, up to 6 months, in the post-COVID time. These long-term symptoms are not only present in severe COVID-19, but also in mild and moderate patients. In addition, recent preliminary data also underlined the presence of long-term COVID-19 symptoms on children and adolescents. The most common reported symptoms after COVID-19 are abnormal lung functions prevalently with persistent dyspnea, general neurological decay, smell and taste disturbances, and chronic fatigue. Other common symptoms include joint pain and chest pain. These symptoms may slow or recur for weeks or months following initial recovery. [9]

-Our study will discuss in next part, that show method and results in Iraqi

patients.

2. Method and Materials.

We conducted a prospective study of 200 Iraqi recovered patients with a spectrum of post COVID-19 symptoms and complications followed up from recovery until these days. A google form questionnaire was performed to collect a required data that included gender of the patients, age, family history, genetic diseases, presence of chronic disease, date of infection, symptoms and complications other additional information and after SARS-2/COVID-19 viral infection in recovered patients. Taken in consideration this study was had important methodological limitations, it focuses on patients in specified areas and age groups. The link of google form questionnaire is https://forms.gle/f3jhSJss5gTUHE4k7 .

3. Results

Out of a total of 200 patients were 127 (63.5%) women and 73(36.5%) men (figure 2). There was a relationship between the presence of other comorbidities and severity of the disease. Also, the severity of COVID-19 was related to the severity of post-COVID-19 manifestations. Only 9% of all subjects have no manifestation after recovery from the disease while a large percentage of subjects suffered from several symptoms and diseases. The most common symptom reported were Anosmia, ageuse, dyspnea, myalgia, weakness, Cough, sore throats, tonsillitis, headache. More critical manifestations like pulmonary disease, hepatic illnesses, renal failure, myocardial complications and immunological problems were reported by a few percent of the subjects as shown below (Table2). About 181 (90.5 %) patients were had no chronic disease and around 124 (62.0 %)

patients without genetic problems.

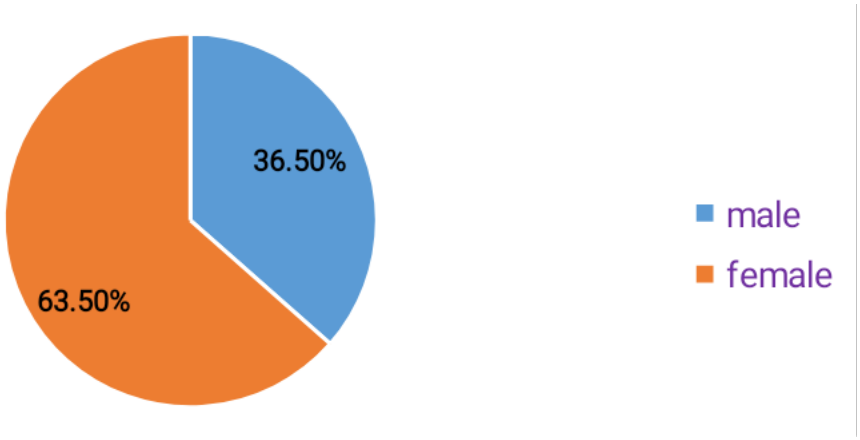

Figure 2: percentage of female and male who participate in this study

Variable	*postCOVID-19*	
Gender	Female	127 (63.5%)
	Male	73 (36.5%)
Age	50≥ yrs.	11 (5.14 %)
	40_49 yrs.	5 (2.33 %)
	30_39 yrs.	10 (4.63 %)
	20 _29 yrs.	74 (80.55 %)
	<20 yrs.	11(5.09%)
Comorbidities (Prior COVID - 19)	Hypertension	24 (12.0 %)
	Diabetes	31 (15.5 %)
	SLE	1 (0.46 %)
	Heart disease	7 (3.50%)
	Fever	20 (10.0%)
	COPD	5 (2.31 %)
	Cancer	5 (2.31 %)
	Depression	3 (1.38 %)
	Kidney disease	3 (1.38 %)
	Asthma	6 (3.0%)
		1 (0.46 %)
		1 (0.46 %)

	Severe menstruation	2 (0.92 %)
	OCD	2 (0.92 %)
	Coronary artery disease	2 (0.92 %)
	IBS	1 (0.46 %)
	Allergic rhinitis	
	GIT disease	
Post -COVID manifestations	Arthralgia	7 (3.5%)
	Back pain	3 (1.5%)
	Arms/legs heaviness	14 (7.0%)
	Weakness	39 (19.5%)
	Cerebral stroke	2 (1.0%)
	Headache	22 (11.0%)
	Myalgia	23 (11.5%)
	Body pain	9 (4.5%)
	Paresthesia	3 (1.5%)
	Attention disorders	2 (1.0%)
	Memory disorders	5 (2.5%)
	Fatigue	11 (5.5%)
	Depression	3 (1.5%)
	Dizziness	2 (1.0%)
	skin disease	3 (1.5%)
	Tachycardia	3 (1.5%)
	Chest pain	5 (2.5%)
	Eye pain	1 (0.46 %)
	Sight impairment	2 (1.0%) 9 (4.5%)
	Anorexia	1 (0.46 %)
	bronchiectasis	1 (0.46 %)
	Skin sensitivity	1 (0.46 %)
	Hepatitis	2 (1.0%)
	Palpitations	1 (0.46 %)

Post -COVID manifestations	Xerostomia	1 (0.46 %)
	Abdominal pain	22 (11.0%)
	Dyspnea	5 (2.5%)
	Weight loss	4 (2.0%)
	Vision disorders	2 (1.0%)
	Pharyngitis	6 (3.0%)
	Rhinorrhea	2 (1.0%)
	Sickness	2 (1.0%)
	Dry cough	5 (2.5%)
	Inability to walk	1 (0.46 %)
	Constipation	1 (0.46 %)
	Diarrhea	47 (23.5%)
	Ageusia	1 (0.46 %)
	Alopecia	23 (11.5%)
	Hair loss	41 (20.5%)
	Anosmia	23 (11.5%)
	Wet cough	1 (0.46 %)
	Importance	1 (0.46 %)
	Otitis	37 (18.5 %)
	Increase body temperature	6 (3.0%)
	Muscle weakness	2 (1.0%)
	Sinusitis	1 (0.46 %)
	Insomnia	3(1.5%)
	Immune impairment	

Table 2. General characteristics of 200 post-COVID-19 patients. (yrs. `Years, SLE: systemic lupus erythematosus, COPD: chronic obstructive pulmonary disease, OCD: obsessive-compulsive disorder, IBS: irritable bowel syndrome).

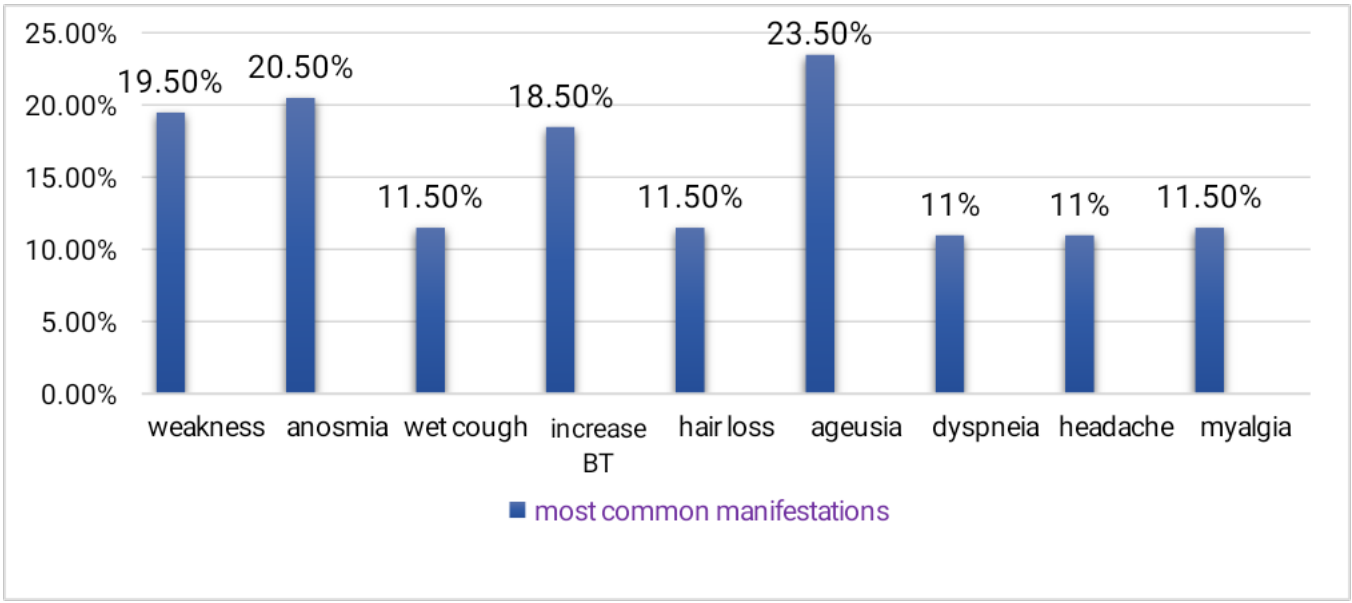

Figure 3. Most common manifestations post recovery of covid-19

4. Discussion.

Based on the data that was collected from google form questionnaire for 200 Iraqi person, who lastly infected and recovered from covid-19. We noticed that only 9% of all subjects have no manifestation after recovery from the disease and another 91% of all subjects have manifestation ranged from mild to severe which need close monitoring. The respiratory system rests the most prevalent system of serious injury outcomes of COVID-19, manifesting as dyspnea, wet and dry cough, sinusitis, otitis, rhinorrhea, pharyngitis and bronchiectasis that occur because the virus causes damage to the walls of the alveolar cells and this results in the formation of debris, which accumulated in the walls of the alveolar cells and causing thickening and this results in lung distress and damage. This damage causes shortness of breath and other symptoms. Lung inflammation or damage can be assayed by CT scans. [10]

The central nervous system (CNS), is the central processing unit of the human system, which can maintain life and homeostasis. The SARS-CoV-2 can enter the CNS via the nasal route and could arrive the olfactory bulb region of the brain to trigger any form of infection. The COVID-19 patients do manifest neurological symptoms such as insomnia, headache, weakness or muscle weakness, ageusia, anosmia, dizziness, memory loss, attention disorder and arms and legs heaviness. The immune system of

brain does not react, if there is any acute, tenacious or dormant form of viral infection inside the CNS, that results in neurological disorders. At this point, the brain damage has yet to be demonstrated as a crucial outcome of the COVID-19 infection. There are theories which suggest that viral infections can trigger a cytokine storm in the brain when the immune system of the host cell over-reacts to the virus. This cytokine storm could release various pro-inflammatory cytokines such as Interleukine-6 (IL-6), Interleukine-12p40 (IL-12p40), Interleukine-15 (IL-15), tumor necrosis factor -alpha (TNF-α), chemokine (C-X-C motif) ligand 9 (CXCL9) and chemokine (C-X-C motif) ligand 10 (CXCL10), which can induce demyelination or cell deaths in the nervous system. [10]

The eyes may have a role in transition of covid-19 to enter the inside the body because the ACE2 is prominently present in retinal pigment epithelial cells of the retina in the eye, which enacts as the functional receptor for the binding of the SARS-CoV-2 to the host cell. The patients who recovered from the SARS-CoV-2 infection might also have ocular related symptoms including eye pain, vision disorder, Sight impairment. As reported 50 years' male suffering from hypertension has glaucoma and vision impairment post covid-19 manifestation. [10]

COVID-19 patients also have an impact on their cardiovascular systems through binding SARS-COV-2 toc ACE2 receptor on heart muscle. This binding could deviate the normal ACE2 signaling pathways consequentially leading to acute myocardial infarction. The alteration in the ACE2 signaling pathway could also arise into acute systemic inflammatory responses and cytokine storm and may cause multiorgan failure or damage in the human system. The cytokine storm can cause an increase in proliferation of cardiac muscle cells and might form a fibrous cap on the fatty steak which results in necrotic lipid core rupture and forms blood clots resulting in myocardial infarction or cerebral stroke. As reported 26 years' female has manifested with cerebral stroke and blindness in one her eyes as result of clotting in blood vessel that supply the eye. Hypoxia during covid-19 infection, which results from increasing in cardio metabolic can impair the myocardial oxygen demand supply and might lead to myocardial injury. As reported also 50 years' male with hypertension has manifested with cerebral stroke. [10]

Patients with post COVID-19 recovery have been known to commonly exhibit GI manifestation include anorexia, constipation, diarrhea, abdominal pain and hepatitis. Diarrhea may occur due to the abundance of ACE-2 in the epithelium of the GI tract makes it vulnerable to the SARS-CoV-2 entry. Studies have shown increased ACE-2 expression in the mucosa of the tongue, esophagus, gastric mucosa, ileum, and rectum. In addition to the above mechanisms, gut flora has been shown to be altered in the patient's severe disease state with the use of antimicrobials, and enteral nutrition. While loss of appetite is a common GI manifestation in COVID-19. Mechanism of anorexia is fairly related to nausea and vomiting, but assessing the literature to evaluate the precise pathophysiology is not available. The precise mechanism of liver involvement in COVID-19 patients is unclear. Various mechanisms have been proposed, one of these mechanism is expression of ACE2 in higher amounts in the biliary epithelium (20 times compared to hepatocytes). When SARS-CoV-2 enters the mucous membranes, it can access the biliary system via the portal vein. SARS-CoV-2 can cause direct immune damage to hepatocytes (cytopathic effect). Direct viral cytopathic with micro vesicular steatosis, mild lobular, or portal involvement has been reported. Cytokine storm noted in COVID-19 patients can lead to excess inflammatory burden and potential immune-mediated damage. Immunosuppressive medications such as calcineurin inhibitors reduce the Interleukin-2 and mycophenolic acid inhibits IL-17, which interferes with T-cell function. Furthermore, passive congestion due to increased use of positive pressure ventilation, drug-induced liver injury from medications (antiviral and antibiotics) commonly used during the course of illness are real possibilities [11]. To check the GI tract inflammation in COVID-19 patients, endoscopy can be recommended for those recovered patients. The enzymes AST and ALT should be checked for possible liver injury and creatinine levels for acute kidney damage. [10]

In our study we noticed that 23 women had manifested with hair loss. In particular, patients with SARS-CoV-2 infection showed a consistent increase in proinflammatory cytokines (tumor necrosis factor α, interleukin 1b, interleukin 6, and types 1 and 2 interferon) which can explain infection-related skin manifestations, such as livedoid vasculopathy, urticaria, COVID toes, and chicken pox–like rash. Cytokine storm can initiate the development of TE by damaging the matrix cells, and usually, the high

levels of interferons have already been confirmed to be associated with ATE. [12]

As reported of 37 years' male had manifested with impotence due to COVID-19 infection could affect male sexual function through endothelial damage in erectile tissue, testicular damage, and psychological alterations. [13]

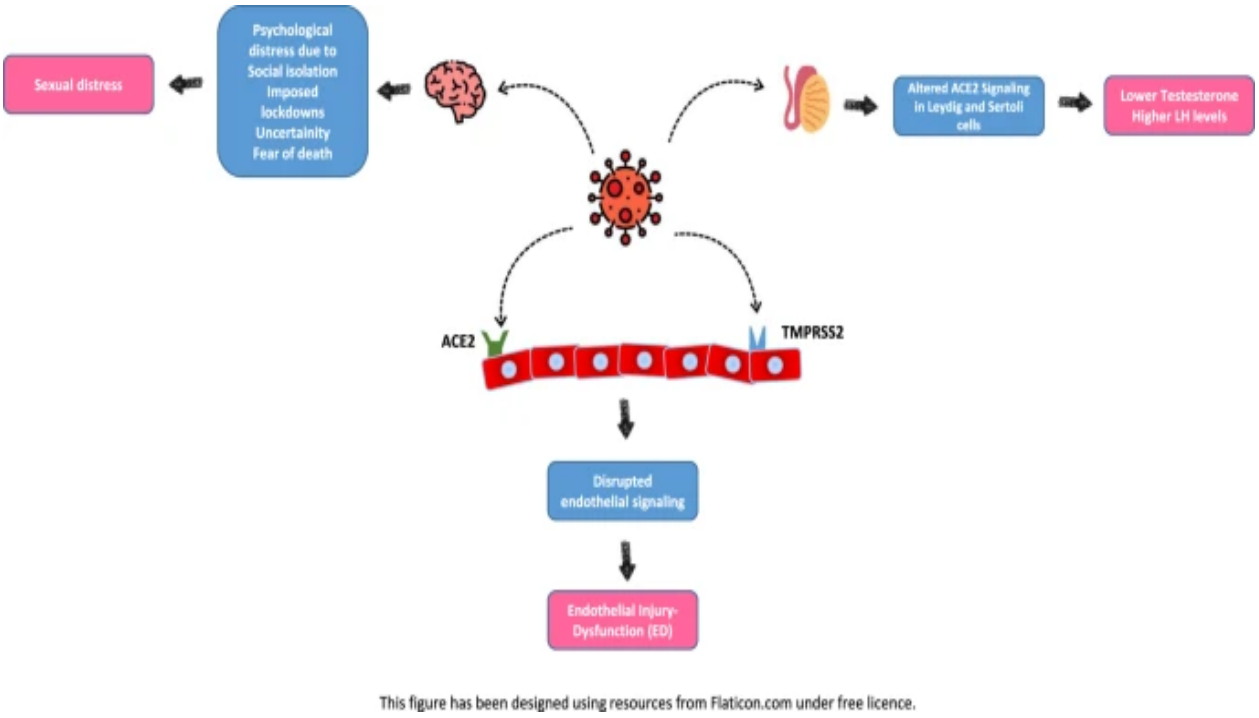

Figure 4: Possible pathways through which COVID-19 causes erectile dysfunction.

Most of the COVID-19 recovered patients are experiencing stress for several weeks and this usually disappear within a short period, but the psychophysical symptoms including depression, fear and anxiety may persist for a longer time. [10]

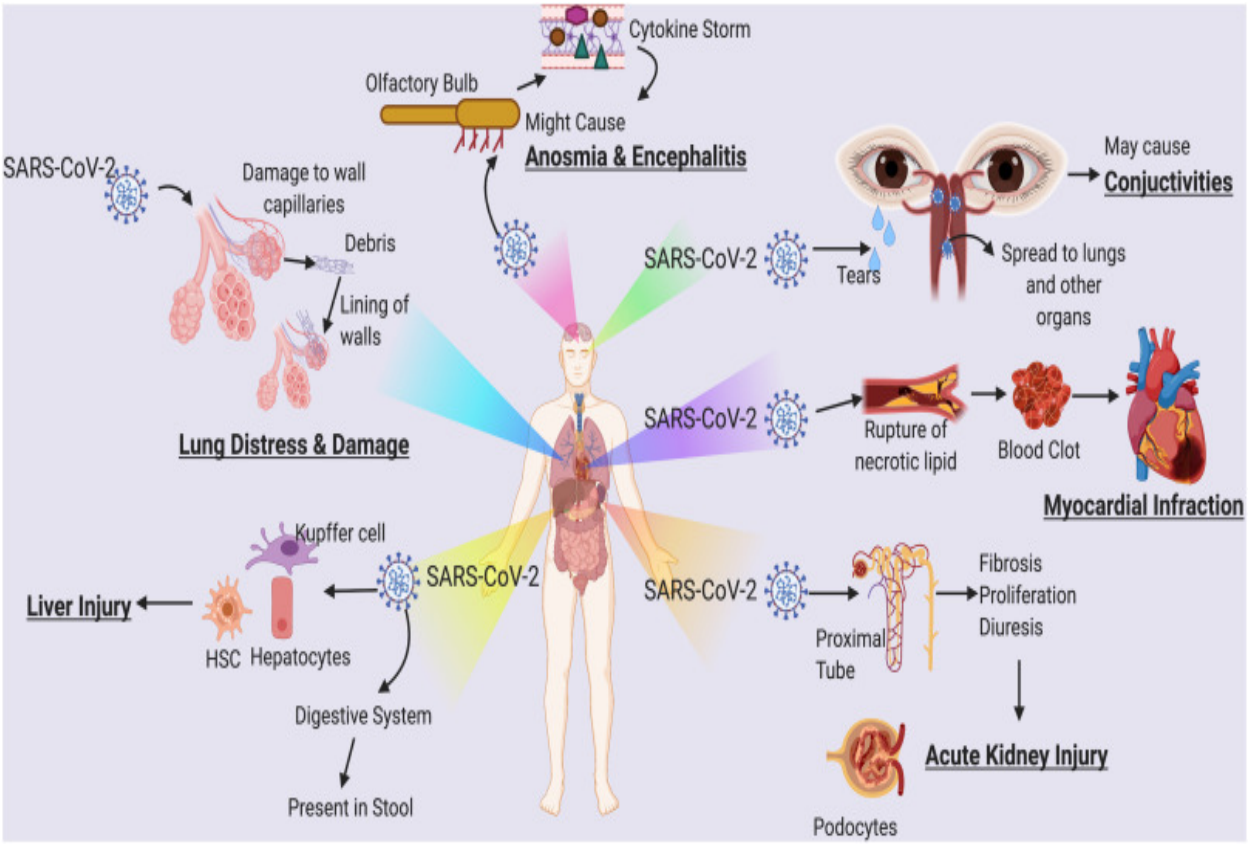

Figure 5: Effect of SARS-CoV-2 infection on organs in different parts of the body.

5.Conclusion

However, COVID-19 is a new disease and uncertainty remains regarding the possible long-term health sequelae. This is particularly relevant for patients with severe symptoms, for whom long-term complications and incomplete recovery after discharge would be expected. COVID-19 has materialized into a deadly disease affecting people worldwide. Besides the common symptoms that occur in COVID-19. It has recently uncovered into a multifaceted condition known to affect various other organs. This disease appears to be at the hub of various converging pathways. Altogether they exhibit detrimental effects on the individual who have infected with the virus. Even though our review suggests that most post COVID-19 sequelae in young, previously healthy adults, there are indications of multi-organ impact .Close attention should be paid to residual impairments in multi-organ function, especially persistent reduce lung functions , mental health , neurological and physical sequelae including post-viral fatigue syndrome What emerges from this review is that the most common reported symptoms after COVID-19 are abnormal lung functions prevalently with persistent dyspnea, general neurological decay, smell and taste disturbances, headache and chronic fatigue. Other common symptoms include joint pain and chest pain. These symptoms may linger or recur for weeks or months following initial recovery. patients with mild-to-moderate COVID-19 the more common long-term symptoms are chronic fatigue, anosmia/ageusia, dyspnea, but also difficulty in concentration, memory loss, and confusion. These symptoms seem to be present in a higher percentage of patients who were initially more ill. Likewise, the general cognitive decay, despite also being present in mild-to-moderate COVID-19 patients, also appears to be more closely related to critical-to-severe forms of COVID-19. Considering the whole overview of widespread long-term symptoms reported in this review the one undeniably most prevalent in mild-to-critical COVID-19 patients is chronic fatigue, weakness, myalgia and insomnia thereby reducing patient's quality of life.

6.Recommendations.

Then, through this follow up study, we supply a few recommendations to preservation the COVID-19 recovered patients as well as their families from the effect of this disease. The recommendations are:

- People who have recovered from COVID-19 should be more careful in maintaining and monitoring their health status. They have to be in regular monitoring for their outlook complications that may take place after their recovery. Those recovered patients are recommended to get CT-scan, and Magnetic resonance imaging (MRI) scans and University of Pennsylvania Smell Identification Test (UPSIT) to test smell identification, as loss of smell is one of the premier symptoms of neuroinvasion in COVID-19 patients.
- The one health connotation stresses the ecological relevance between human, animal, and environmental health. Understanding the importance of microbiome relevance between the environment-humans-animals opens up the potential for innovative and integrated approaches to diagnosis, treatment, and intervention of diseases to animals and humans.
- Counselling is proposed for the recovered patients periodically not to lose courage and keep themselves mentally strong.
- The host genetic capability and biomarker genes in different populations with respect to viral infection and persistence will help in understanding the co-evolution of the coronaviruses and other age-old diseases like Malaria etc. This will also help to dissect the genomics of symptomatic and asymptomatic cases.
- Recovered patients should be heartened to share their feelings about the treatment, quarantine, symptoms of the disease and their experience on the whole to reduce their psychological burden.

- Home monitoring programs for recovered patients can help them to promote their diet and physical activity.
- Tighter supervision of workplace safety should be equipped to safeguard the safety of people's lives, along with the COVID-19 recovered patients. [10]

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