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Study the susceptibility of infection with Hepatitis type C for Covid – 19 patients in Baghdad District – Iraq

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Abstract : The corona virus as mentioned as SARS-Cov2 is a respiratory disease that causes a respiratory diseases and main responsible for the pandemic of corona in 2019 which started in Wuhan city- China and dispersed to the worldwide cases a million of infection among people in different countries, this study to showed the relationship between the patient infected previously with SARS-CoV2 and the possible infection to Hepatitis virus type C, the main causes of acute hepatitis. The patients tested from AL Yarmouk Hospital- Baghdad and ranged between 19-74 years old from both genders. The result showed no susceptible infection between the HCV disease and previous infection with corona disease.

Keywords:

Introduction

Coronaviruses are a huge groups of viruses that initiate symptoms ranging from the flu like cold to more dangerous respiratory diseases (1).Coronavirus disease 2019 as given abbreviation as (COVID-19) is a unique highly contagious strain of this virus obtain their name from world health organization(2).first diagnosed in Wuhan, China, in late December of 2019(2).this virus represent most strains of viral families that causes severe acute respiratory associated syndrome. The main causes of SARS outbreaks that occurred in 2004 releated to this family of corona viruses, so because of many species can causes an outbreaks among years the SARS causin virus given a name SARS-CoV-1 .(3)while the viral species of this family that causing the Covid-19 outbreak in 2019 given a name SARS-Cov-2 (4). Previously, this virus was called 2019 novel coronavirus (2019-nCoV), It is also known as the human virus, and it is called (HCoV-19 or hCoV-19)(5).

After massive transmission of virus from site of infection in Wuhan city to different countries and the highly acceleration in infection among the people, The World Health Organization declared a global health emergency of concern on January 30, 2020, following the declaration of the disease pandemic on March 11. (6). Corona virus transmitted through the cough droplet from infected person to healthy person (7).based on evidence gathered from infected person, this virus was primarily transferred mainly through the droplet and other contact (8). Transmission may reach to distance between two persons to nealy 2 meters can successfully achieve the transmission(9). Close contact between the people may cause the transmission specially indoor (10). Signs of Symptoms are likely to appear from four to five days after infection (11). One of the important notes that aid the virus to rapid transmitted through people that asymptomatic patient can spread the disease to other people, the virus first accumulate in the upper respiratory tract (12).estimated duration of viral infection between 10-20 days till the shedding of virus out of patient, this duration may be increased with patient develop severe Covid infection or with immunocompromised patients (13). There is a difference in the size of viral particles up to the smallest size aerosols that remain air tangled or may be a large droplets that airborne handled but don't travel to far distances, these droplets become more concentrated in air when people become more closely approximately which ease the transmission of virus and accelerate the infection rate between the people and community, also the ventilation play an important roles in preventing of transmission because its reduce the duration of droplets to remain in the air from hours to (14) . The disease spreads widely in groups, and this spread indicates a specific indicator or a specific geographical location, (15)where large groups are infected by one host. (16). Corona virus is enveloped capsid has a single stranded RNA with positive sense non (17). The diameter of this virus is 60–

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140 nanometers in (18). The spherical shape of capsid has 4 main structural components involved spikes, envelope, membrane and nucleocapsid (19). Corona family composed of four main genera; α, β, γ, and δ based on their genomic structure. α and β coronaviruses infect only mammals(20). SARS-CoV-2 is a β-coronavirus like the viruses that cause SARS. It is possible for a person to carry the virus for a period ranging from two days to two weeks before any symptom is diagnosed on the person (21). Many factor affecting the possibility of infection with corona virus including the age, immunity which show a big difference in the severity of infection among the people (22). The infection with corona has three stages of symptoms, the first stage can be categorized by sore throat accompanied with headpain, muscle pain and chills, reiterated shaking with chills while the second stage of symptoms The second stage of the symptoms appears in the form of severe fatigue, a strong cough, shortness of breath, loss of the sense of taste and smell, a gradual rise in temperature, but in the case of diarrhea, the infected person enters the third stage, which is also accompanied by difficulty breathing, blue lips, chest pain(23). Anosmia which mean loss of smell and ageusia refer to loss of taste represent the more frequent identified signs of novel corona virus infection which associated with other common symptoms of disease like such as fever, cough and dyspnea(24). In people who do not suffer from previous disorders in the larynx and the nose, they appear to lose their sense of smell and taste when infected with this virus as 88% of symptomatic cases(25).

Some of the clinical features shown by a (chest computed tomography scan) This examination shows the defect that affects the respiratory system, heart injury, and acute pneumonia, which in turn leads to death. (26). Other cases lead to shortness of breath and damage to the respiratory system, in addition to the appearance of symptoms of the digestive system, such as diarrhea. (25). About 81%people suffer from these symptoms slightly, while a 14% percentage suffer from severe symptoms, but this 5% percentage is the most harmful person, and they must go to the hospital for the intensive care unit because of kidney failure and the inability to breathe (27).

There are people who do not show symptoms clearly all the time(28). As for people who do not show any symptoms, they only carry the disease and spread the disease quickly(29), and some of them show symptoms at a later time of infection. This condition is called "pre-symptomatic"(30). As a result, from mentioned before, there is delayed time between the time of infection and appearance of symptoms which may 4 to 5 days(31). possibly being infectious on 1 to 4 of those days(32). In some cases, the symptoms appear after twelve days of first infection , in contrast some people showed the initial onset of dymptoms appear after seven days of onset of viral transition’s (33). Some people with severe cases of this virus recover well, and some people recover, but symptoms of fatigue remain for several months. (34)Some people suffer from long-term organ damage, so that full recovery from this virus is difficult(35). Many researchers found that the most common symptom of infection with this virus is respiratory symptoms, and I also found research that invades the nervous system(36), and some researchers showed that the virus infects the liver, with a ratio of 2-10 people suffering from diarrhea, and the virus was detected in blood and feces (37).

This proof associates the ability of viral exposure in the liver, both SARS-CoV-2 and SARS-CoV bind to the angiotensin-converting enzyme 2 (ACE2) receptor to enter the target host’s cell (38). Then the virus multiplies later and infects other cells in the upper part of the respiratory system and lung tissue, then the patient develops symptoms and clinical manifestations.because the virus utilize the angiotensin-2 converting enzyme (ACE2) receptor protein to attack the host system(39).

The cell entry receptor, ACE2, is widely expressed across the human body, including the hepatobiliary system (hepatocytes and cholangiocytes), Digestive system (esophageal epithelial cells and sucking intestinal cells of the ileum and colon), lungs (type II alveolar cells), cardiovascular system (heart muscle cells), renal system (proximal tubular cells and urinary bladder cells) and pancreas (40).

Studies have observed that ACE2 expression in the cell clusters of cholangiocytes was notably greater than that in the hepatocytes population with approximately ration 59.7 % vs. 2.6% (41).

The authors has conclude that SARS-CoV-2 may directly bind to ACE2 positive cholangiocytes, but not hepatocytes, to exert a cytopathic effect. Cholangiocytes are involved in many aspects of liver physiology, including regeneration and adaptive immune response mechanisms, and the disruption of cholangiocyte function can cause hepatobiliary damage. This is supported by cholestatic markers, including gamma-glutamyl transferase (GGT), that can be found in some, but not all, case series of COVID-19(42).

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Particularly, a recent review reported unpublished preprint data with GGT elevations in 54% of cases(43).
It was found that the cells lining the bile juice contain more receptors for the ACE2 than the liver cells , Which is the cause of liver weakness due to bile juice damage (44) .
In a human organoid model of liver ductal organoids, permissiveness to SARS-CoV-2 infection was observed. Cholangiocytes affected directly through dysfunction of their barrier and bile acid transportation under viral infection through dysregulation of genes involved in tight junction formation and bile acid transportation, supporting the susceptibility of cholangiocytes in SARS-CoV-2-related liver injury(45).
In hepatitis, immune cells are triggered to secrete cytokines, which later act as a driver of liver injury for various reasons (46)It was also found that there is a close relationship between lymphocytes and hepatic injury. The less lymphocytes, the more obvious liver injuries(47).
Hepatitis C virus as abbreviated as (HCV) infection represent one of most important agents causing the bloodborne infection in the united states and also playing a magical role in the liver morbidity and mortality (48). The World Health Organization has shown that (71 million)people in the world are infected with hepatitis C virus, which is the same to one percent of the world's population, 10-20% of people infected with viral hepatitis C have cirrhosis, and 7% develop hepatitis. viral infection of hepatocellular carcinoma (49 ,50).

Material and Methods

Procedure

Blood samples has been taken from the patient's median cubital vein prior sterile area by alcohol (Ethanol) then insert the sample into the gel tube then putting the tube into the centrifuge (3500 RPM) for 5 minutes after that take off the tube from the device, use the pipette to take 3 drops of serum (approximately 75 µl) to the sample well (HCV Kit), this HCV Kit procedure (The Hepatitis C Virus Rapid Test Device detects antibodies to HCV through visual interpretation of color development in the internal strip. Recombinant antigen corresponding to Core, NS3, NS4 and NS5of HCV is immobilized on the test region of the membrane. During testing, the specimen undergoes a chemical reaction with HCV antigens that already precoated onto the sample of test which conjugated to colored particles. This mixture is transmitted in membrane by capillary form to reach and interact with the reagents. If the color of the strip changes, it indicates that an infection has been found, i.e. the presence of antibodies to this virus. As for the absence of the color of the strip, it indicates a negative result, The appearance of the colored band near the control area indicates that the quantity added to the test (sample) is the required quantity.

Patients

Patient previously infected with covid-19 aged between 19-74 from two genders male and female, these patients hospitalized in AL-Yarmouk hospital -Alkarkh, districts-baghdad, patients infected with covid-19 between November 2021 and March 2022. The sign of infection ranged between moderate to severe. The site of sample collection represents a center for most corona virus infection records in Baghdad district to make sure of quality and ensure if there is any relation between the covid and hepatitis c virus which is. All sample have been taken from patient from Baghdad – alkarch district of city, nearly 51 patients test for HCV tests, 5 patient tests as control whose don’t infect with covid-19. Among the total number of patient 46 Patient tested positive for covid-19, al necessary information from patient like age, time of infection and duration and severity of disease has been recorded.
People infected with this virus show symptoms from mild to moderate to very severe symptoms, After the infection, from two to fourteen days, symptoms appear, which include respiratory symptoms, cough, shortness of breath, headache, muscle pain, nausea, severe moderate diarrhea, depending on the condition, weight loss, continuous fatigue and thinness, As for the elderly, the symptoms are very strong, especially people who suffer from chronic diseases, kidney failure, or weak heart muscle.

Result

The 46 patients infected previously with covid-19 showed negative test for HCV test in all patients when they undergo a blood test for the hepatitis C virus as showed in table 1.

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Table 1 HCV test for Covid-19 patients

Sample No.	HCV RESULT	TYPE OF SAMPLE	TREATMENT	SEVERITY	HOSPITALIZATION	VACCINE	GENDER	AGE	TIME OF INFECTION
1	NEGATIVE	WHOLE BLOOD	yes	MILD	NO	PFAIZER (AFTER INFECTION)	MALE	74	2
2	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	MALE	62	6
3	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER(AFTER INFECTION)	MALE	62	4
4	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	35	5
5	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	NO	FEMALE	72	3
6	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	62	4
7	NEGATIVE	WHOLE BLOOD	YES	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	19	4
8	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER(AFTER INFECTION)	FEMALE	27	4
9	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	NO	FEMALE	26	6
10	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	PFAIZER (AFTER INFECTION)	MALE	28	2
11	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	PFAIZER(AFTER INFECTION)	FEMALE	26	6
12	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	23	5
13	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	63	7
14	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	40	6
15	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	41	6
16	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	ASTRAZENKA (AFTER	MALE	43	4

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						INFECTION)			
17	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	49	6
18	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	MALE	54	3
19	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	NO	FEMALE	27	4
20	NEGATIVE	WHOLE BLOOD	YES	MILD	NO	NO	FEMALE	48	3
21	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	CENOFARM (BEFORE INFECTION)	FEMALE	32	2
22	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	NO	FEMALE	25	4
23	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	NO	FEMALE	75	5
24	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (BEFORE INFECTION)	FEMALE	24	4
25	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	PFAIZER (AFTER INFECTION)	FEMALE	52	3
26	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	PFAIZER (AFTER INFECTION)	MALE	37	7
27	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	40	5
28	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	CENOFARM (BEFORE INFECTION)	FEMALE	53	6
29	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	23	4
30	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	FEMALE	64	6
31	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (AFTER INFECTION)	MALE	31	3
32	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	PFAIZER(AFTER INFECTION)	FEMALE	32	4
33	NEGATIVE	WHOLE BLOOD	NO	MILD	NO	PFAIZER (BEFORE INFECTION)	MALE	33	3
34	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	PFAIZER (AFTER	FEMALE	47	5

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						INFECTION)			
35	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	NO	MALE	38	4
36	NEGATIVE	WHOLE BLOOD	YES	SEVERE	YES	ASTRAZENKA (AFTER INFECTION)	FEMALE	50	5
37	NEGATIVE	SERUM	NO	MILD	NO	NO	MALE	27	4
38	NEGATIVE	SERUM	YES	MILD	NO	PFAIZER(AFTER INFECTION)	MAIL	23	3
39	NEGATIVE	SERUM	YES	SEVERE	NO	NO	FEMALE	23	4
40	NEGATIVE	SERUM	NO	MILD	NO	CENOFARM (BEFORE INFECTION)	MAIL	26	5
41	NEGATIVE	SERUM	YES	SEVERE	NO	PFAIZER(AFTER INFECTION)	MAIL	23	6
42	NEGATIVE	SERUM	YES	SEVERE	NO	PFAIZER(AFTER INFECTION)	MAIL	24	5
43	NEGATIVE	SERUM	YES	SEVERE	NO	NO	MAIL	26	3
44	NEGATIVE	SERUM	YES	SEVERE	NO	PFAIZER(AFTER INFECTION)	MAIL	28	3
45	NEGATIVE	SERUM	NO	MILD	NO	NO	FEMALE	20	3
46	NEGATIVE	SERUM	YES	SEVERE	NO	CENOFARM (BEFORE INFECTION)	FEMALE	28	2

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Picture (1) Collection of blood from patients and tested for HCV infection

Discussion

Based on many studies showed that corona virus has a trophism to ACE-2 receptor as a main point of entry to the target cell (51). The cholangiocytes expressed ACE2 receptors on their surface which made these cells of liver susceptible to infected with corona virus (52) many surface proteins aids virus to enter the host cells like transmembrane protease serine 2 (TMPRSS2) which is suggested to affect the S protein at the cell surface and induces SARS-CoV-2-cellular membrane fusion(53). Most important point has been diagnosed in patient infected with HCV showed high expression of TMPRSS2 which may lead the inflated SARS-CoV-2 infection in these patients (54). next issue concern the relation between the infection with HCV and corona , HCV is a systemic disease, associated with significant extrahepatic morbidity despite that can occur independently of liver injury(55).many reports has revel a many HCV antibodies seropositive have linked to nearly one and half folds of possible increasing in the mortality of liver (56). The detection of circulating immune response in HCV patients show similarity with patient infected with corona virus only may indicated the mechanisms may involve the induction of circulating immune complexes and immune-mediated cellular toxicity, which is reported to occur in SARS-CoV-2 and may be related to the potentiated effects on the virus in HCV patients. Third issue, there seems to be an immune response intersection between chronic HCV and SARS-CoV-2 infection (57). Studies have shown an association between the production of cytokines as INF-γ and TNF-α responsible for the production of inflammatory cells and progressive liver injury in chronic hepatitis C infection.

While the production of cytokines as IL-4 and IL-10 may modulate the production of immune cells modulating the inflammation caused by the virus. The death case of COVID-19 has shown an indication of liver disease in ration between 58% to 78% (58). More than 20 publications to date reported abnormal levels

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of aminotransferases in patients with COVID-19 (59). A recent systematic review and meta-analysis on LFT abnormalities provided a pooled elevation of aspartate aminotransferase (AST) in 33.3% and alanine aminotransferase (ALT) in 24.1% of cases (60). Many studies has shown a correlation or intact relationship between the severity of corona virus infection and the liver dysfunction (61). On the other hand, mild and moderate cases experienced only discrete abnormal LFT values. Older age patient with covid -19 also express highly liver injury that other age of patients based on current reports that surveillance the progression state of covid-19 patient symptoms. Based on these case series, patients with severe COVID-19 and pre-existing liver conditions(62) but also elderly patients should undergo surveillance and individually tailored therapeutic approaches for potential liver injury (63). Like in SARS-CoV and MERS-CoV infections, abnormal levels of albumin and lactate dehydrogenase (LDH) were also reported in SARS-CoV-2 infection, with the maximum of 98% and 76% of the patients affected as reported in the study by Chen et al (64) not always should recommended the level of LDH and AST because their elevation may as a result of muscle damage (65). A high level of cytokines in people infected with this virus, which is highly associated with mortality, and a current study showed that a high level INF-γ, leads to death in these patients with this virus (66). Cytokines response of TNF and IL-10 stimulation may indicate that patient with HCV could releated to high mortalilty in patients when infecting with corona (67). The development of fibrosis in the liver and the rapid increase in atherosclerosis is a result of the failure of the vascular endothelium to function normally due to the presence of a virus SARS-CoV-2 viruses. (68) new pathological reports the causes of endothelitis as result of accumulation of inflammatory cells showed an presence of viral elements in the endothelial cells of corona patient (69). One of the important things is a complete immune response and the elimination of the virus is a healthy immune system and the function of the lining is also intact (70).

Conclusion

The patients whose previously infected with corona virus may susceptible to infect with HCV disease that may developed to hepatocyte carcinoma due to direct relationship between the binding of ACE-2 receptor founded on the hepatocyte cells and the corona virus, also the drugs have been taken by patient during the infection period of the corona disease may effect indirectly with the function of liver so we recommended to routine investigation concern the susceptible infection with HCV specially for elderly patients whose had a respiratory disease caused mainly with corona virus and suffering from moderate symptoms .

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Appendix