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Severity of COVID-19 and Liver Diseases

Kritika Upadhyay, Pramita Muntode*

Department of Community Medicine, Jawaharlal Nehru Medical College, Datta Meghe Institute of Higher Education & Research, School of Epidemiology & Public Health, Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, Maharashtra, India

ABSTRACT

Background: COVID-19 or Coronavirus disease 2019, the emerging pandemic grappled the whole world and turmoil was seen all around the world. Since its inception, it spread to every nook and corner of the world affecting almost everyone mostly in negative way. The hazard that the novel Coronavirus swept through its power of creating fatal medical results and extraordinary infectious made it a, once in a century clinical emergency and hence was declared as public health emergency of international concern by the WHO. No such occasion in the last 100 years of human civilization had been so destructive in the past.

Summary: Along with COVID-19, liver ailments were widely occurring around the world and were considered as one of the worst co morbidity to have. Liver is the largest auto regenerative organ in our body, but COVID-19 affected it in an extremely adverse way. The crucial functions the liver performs must be continuous and hence uninterrupted monitoring of the liver enzymes, which are the indicators of the patients deteriorating condition can help and aid to reduce mortality.

Conclusion: Liver ailments by itself are a serious topic that whole world was worried about, the future course of these ailments such as liver cirrhosis and fatty liver. COVID-19 aggravated the existing condition. Liver ailments and COVID-19 show bidirectional relationship aggravating each other. Yet, more data is needed to support the claim of the bidirectional relationship of the liver ailments and COVID-19. Close monitoring of the patients is essential considering the unpredictable nature of the constantly mutating novel Coronavirus.

Key words: COVID-19, Liver ailments, Liver transplant, AST, ALT, SARS

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Corresponding author: Dr. Pramita Muntode
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INTRODUCTION

Coronavirus disease 2019 or COVID-19 is the ongoing pandemic that has grappled the whole world. Within a span of weeks, it has spread through the world after its inception in December 2019. Initially it was thought that an unnamed pneumonia but later it was found out that it was caused by the novel Coronavirus, which is the latest entrant in the Coronaviridae family of viruses. In past, outbreaks such as Severe Acute Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS) have occurred due to the previous strains of novel Coronavirus.

Since its inception in Wuhan city of the Hubei province of China, it has spread with extremely fast pace [1]. Every person has experienced the brunt of the pandemic in one way or the other. Millions of people got infected with this virus and unfortunately some of them met with fatal clinical outcomes. Till November 24th, 2021, 260,092,573 infections have been registered worldwide and 5,183,321 case fatalities happened due to COVID-19 related complications [2]. The crossing of unfortunate mark of five million case fatalities underlines the deadly nature of the virus showing its ability to create any complications in the person's body [3-5].

Various vaccine makers got approval from the drug controller agencies around the world and many of them began vaccination drive for adults. Vaccination drive for children is still under trial and it will take some time for the vaccine for adolescent candidate. Till now 7,527,195,943 jabs have been given to the people which will protect them from being severely ill [6].

LITERATURE REVIEW

The incubation period of virus is of 2 to 14 days and it generally shows symptoms from second to fourth day from the infection. Basic symptoms include fever, cough, cold along with diarrhea, dyspnea. These symptoms vary a lot considering the patients clinical history. Also, the CT value or critical threshold value can show if the viral load is high or low. Lower is the CT value higher is the viral load and vice versa [7-9]. High viral load can make the clinical

management of the patient difficult and requirement of sophisticated medical care such as intensive care unit, oxygen support system, mechanical ventilation etc. can increase. Comorbidity can decide the course of the treatment and in most of the cases clearly indicates the worse scenario in the patient. Comorbid patients tend to show the severe symptoms and in most of the cases and finally meeting with fatal clinical outcome. Need of the tertiary level medical care is extremely high among such patients. Various comorbidities like liver ailments are some of the chronic diseases that have widespread prevalence among adult population. They are already in an immunosuppressive state and COVID-19 can easily penetrate the cover of weak immune system [10-12].

The hazardous outcomes that novel Coronavirus has resulted through its power of creating fatal medical results and extraordinary infectious biology makes it a 'once in a century' clinical emergency. No such occurrence in the last 100 years of human civilization has been so destructive as COVID-19. Many individuals think that the novel Coronavirus is new virus and it is identified and named with the pandemic of COVID-19. But in fact, Coronaviruses were identified long ago in mid-1960 [13]. In Europe back then, there was an occurrence of cough, fever and cold along with other symptoms among people dwelling in some nations of European continent. When the cases started increasing and almost every person was tested and diagnosed with certain ailments. The screening then identified that there is new viral strain that has not been yet registered. Though the virus was extremely inactive and was not responsible for causing any major destruction to the infected person, but the study was necessary for research reasons [14-16].

Various antibodies test has been done and most of the people showed presence of antibodies in the screening test conducted all over Italy. This meant that they were infected by the virus and now immune system has developed antibody for them. The virus was named as Coronavirus of human strain. Bats and other wild animals were known to be the harbor of this virus and after spill over event; it got transmitted to the humans *via* intermediate animals. The shape of the virus was crown shaped which were spike proteins [17-19].

Pre-existing liver ailments among population

Liver ailments are common around the world especially after industrial revolution when commercialization rose rapidly across the globe. It is common occurrence among adult population of the world. Millions of people suffer from various hepatic disorders like liver cirrhosis, fatty liver, disturbed levels of alanine aspartame and so on [20-22]. These diseases are of chronic type are often derived from lifestyles changes. Consumption of high sugar and high salt foods along with chronic consumption of alcohol and derived products. These individuals are highly vulnerable to any kind of infection as they are going through immunosuppressive state. Already millions of people are undergoing medical intervention as the severity of the disease increases and increasing age makes it even worse [23]. Uncontrolled level of bilirubin levels is also a cause of concern. Prevalence of preexisting Liver ailments around the world is high among the general population especially in the adults [24].

Comorbidity and its correlation with COVID-19

Coronavirus disease 2019 or COVID-19 has resulted in more than five million deaths according to the central repository that collects data around the world. The reason behind its highly fatal nature is its epidemiology that can create unmanageable clinical complications. After almost more than 2 years of its advent, various studies have confirmed that certain sections of population are more vulnerable than others [25]. These are person with underlying chronic illness also known as comorbidity, elderly people, pregnant women and comorbid young adults. Comorbidities such as diabetes mellitus, obesity, liver ailments, renal failure, persons on dialysis support, various cancers and tumors are some of the illnesses which one should not have along with COVID-19 as it creates unmanageable medical complications. Comorbidities have devastating impact on the COVID-19 patients as the comorbid patients have presence of more oxidative stress which is detrimental to the body of the patients concerned. When novel Coronavirus enters such a person's body it creates more oxidative stress and inflammation accentuating the existing problem. The size of the novel Coronavirus is smaller than the human cell and it can easily penetrate the protective cell layer and can take control of the host, with the help of the Angiotensin Converting Enzyme-2 (ACE-2) receptors which acts as a gateway for the virus. All the important tasks assigned to the human cell of the body which is called as a basic building block of life highlighting its important, which is then stopped and cell bursts after the virus population in the cell exceeds its capacity. Various studies have indicated that co morbidity is linked with the requirement of the sophisticated medical care like mechanical ventilation, intensive care unit; oxygen support requirement etc. is high among this section of population. Also, majority of the case fatalities consisted of the comorbid patients owing to the complications created by the Coronavirus diseases 2019. It is important to create more research based inferences on this linkage as more than 40 percent of the world's population is suffering from one or the other chronic illness. This is considerable amount of population to be risked to expose it to the infection of COVID-19 [26-29].

Liver ailments and COVID-19

As mentioned previously Angiotensin Converting Enzyme-2 (ACE-2) receptors is present on various vital organ system of the human body and the liver also harbors such receptors which in turn acts as the entry point for the virus to enter the cells concerned. Liver damage of the COVID-19 patients can happen irrespective of whether it previously had any history of liver ailments or not. A study has found that Alanine Amino Transferase (ALT) and Aspartate

Aminotransferase (AST) enzymes which are most vital serums present in the liver which controls majority of the liver function. Liver basically turns the glucose in to glycogen along with other important functions [30]. These levels were elevated in 14 to 53% of patients who were admitted to the hospitals complaining of the COVID symptoms.

Males were observed to show more elevated levels of these enzymes than their female counter part and severe patients saw a marked increase in their levels than milder patients. One of the studies which had a considerable number of subjects with liver ailment from China there a cohort of 1099 patients was studied for the effect of COVID-19 on liver disease. It showed that 21% of the patients admitted complain the COVID-19 symptoms were having hepatitis B which is generally considered as non-life threatening medical condition but delay in seeking the medical intervention can result into more complications. AST elevation was seen among almost 22% of the patients and ALT levels were surged among % of patients. There was also a marked difference in severe COVID-19 patients and milder ones. As severe patients show elevated levels of ALT elevation than non-severe patients and likewise for AST levels. More than 76 patients showed abnormal bilirubin levels [31].

Biopsy of the specimen of the liver of patients, who met with fatal clinical outcomes due to liver injuries, revealed that the injuries to the liver post COVID-19 infection could be the result of the infection by SARS-CoV-2 or the adverse drug reaction which was used in the treatment of the COVID-19. Severe inflammation is caused by COVID-19. To control the severe inflammation, the innate immune response overreacts and starts killing the healthy cells along with the harmful microorganisms, this can induce multi organ failure. Various biological markers such as C Reactive Protein or (CRP) levels, D dimer, Interleukin 6 (IL 6), Interleukin 2 (IL 2) were found to be elevated among COVID-19 patients. Hepatic cells especially biliary epithelial cells have abundant amount of the ACE-2 receptors which can result into direct infection in liver cells. Complete lack of oxygen intake which happens after hypoxia also known as anoxia is observed to be happening resulting respiratory failure. Drug induced liver injury has been found in some of the patients after usage of lopinavir, ritonavir, remdesivir, chloroquine. Generally long term consumption of several drugs can induce liver injury. Higher antibiotic drugs which are used in treatment of COVID-19 can cause liver injury. Pre-existing liver diseases have chances of reactivation and can impact the patient in adverse way [32-34].

A study conducted in China among the patients recovered from COVID-19 suggested the presence of multi organ injury among severely ill COVID-19 patients. Pigmentation on skin and dark spots suggested the damage of organs especially on liver. Sometimes the liver insult might not seem significant or at times it can be completely camouflaged under various conditions. It is important to check for the serum level deliberately in order to detect the anomalies which are arising out of the COVID-19 [35].

Another cohort study confirms the importance of monitoring of the AST and ALT levels in the COVID-19 patients. A cohort study of 5700 patients having Coronavirus disease 2019 suggested that there was marked abnormalities among the 2176 patients in ALT levels whereas the AST levels were disturbed in 3263 patients. Another important aspect in COVID-19 patients is its inflammatory response is, it causes liver injury and the main reason behind this process is the Systemic Inflammatory Response Syndrome (SIRS). The unpredictability of the COVID-19 can be seen from various examples where the patients initially shows improvement but eventually slips into critical zone due to multi organ failure [36].

Mortality rate more among male than females

As the infection progresses and additional research are being carried out, results of the same are being released; it has seen that a greater number of males are fatally affected by the COVID-19 infection than female counter part. This is attributed to various reasons which pans across the spectrum. But central reason behind this pattern is excess consumption of alcohol and other intoxicating substance affecting the liver in the adverse manner [37]. Various studies prior to the COVID-19 have found that there is widespread prevalence of the chronic consumption of the alcohol among men, while in female the same percentage is comparatively less reported and therefore injuries to liver such as liver cirrhosis, fatty liver occurs more among men than in women. As these diseases make inroads in the human body, it creates more oxidative stress and inflammation on the vital organ like liver and all the immune system starts to repair the losses made by the disease. If such patients which has preexisting liver ailments contracted COVID-19, then already weakened immune system cannot bear the stress induced by the novel Coronavirus and succumb to the pressure [38].

Liver transplantation and COVID-19

Organ transplantation in general and particularly, liver transplantation is one of the most overlooked aspects of the impact of COVID-19. Various patients suffering from major terminal diseases and there is no chance of improvement in their condition in case of organ failure, it is suggested that the person should get the replacement from the suitable donor.

It is seen that the habit of over consumption of alcohol can be dangerous as it can create several ailments not just related to liver but to kidney and other gastrointestinal issues. Therefore, it is important to completely abandon the habit of consumption of alcohol as it is doing more harm than good. Proper de addiction facilities should be chalked out across the country in order to ensure safe and gradual de addiction of the addict. Increase in domestic violence is also a major issue as lockdown induced closure of the liquor shops made the addicts even more raged. Counseling and telemedicine

can be effectively used in order to carry out the procedure [39,40].

Preventive measures for comorbid patients

As it is seen that in case of Coronavirus disease 2019 or COVID-19 there is no exact course of treatment available that will be used for everyone and which will have the capacity to cure the diseases because of the novelty of the disease. Hence it becomes important to look at other measures rather than curative measure which are preventive measure.

DISCUSSION

Preventive measures focus on the aspect of preventing the disease from happening at first place. As we have already seen that novel Coronavirus disease 2019 creates unprecedented complications among the infected patients which is often becomes clinically unmanageable. Also, there is the new phenomenon called long COVID-19 in which patients experience the symptoms of the disease of COVID-19 even after getting discharged from the same. Also, the patient suffers a lot of psychological issues which comes up with COVID-19. It is seen that long durations of isolation and quarantine can affect the patients psyche in an adverse way. All these can be bypassed and one can protect itself through various ways which are together termed as preventive measures. These measures include wearing masks of appropriate feature, maintaining minimum physical distancing of 2 meters, not going outside if not necessary as it will protect one from airborne virus, vaccination, regular sensitization of hands and so on are some of the measures which can one easily imitate and be protected from novel Coronavirus. These measures hold good value as these measures and methods are tried and tested in previous outbreaks like SARS, MERS, Ebola, Swine flu etc. All these measures were found to be beneficial. In case of Ebola which was initially an unknown disease, took tolls of doctors and health care professionals treating the Ebola patients. But after the usage of the masks and proper sanitization methods, the mortality rates among doctors and other professionals came down drastically. The concept of critical threshold in COVID-19 is extremely important as it shows the quantity of the viral load present in the human body. Therefore, one must ensure to follow all these guidelines at all cost.

CONCLUSION

Liver ailments was itself a serious topic that whole world was worried about the future course of these ailments such as liver cirrhosis and fatty liver. COVID-19 aggravated the existing condition. The bidirectional relationship between liver ailments and COVID-19 in which pre-existing liver diseases can aid the proliferation of COVID-19 and COVID-19 can induce liver injuries to the COVID-19 patients. Therefor it is very much important that the health care personnel must monitors vital serums associated with such as AST and ASP levels, CRP, D dimers can also help to detect the liver injury. Liver is one of the most important organs of the human body as it converts food to the substance which the body requires. Preventive measures are extremely cost effective yet beneficial way of controlling the viral spread. It must be encouraged along with vaccination as it also provides considerable amount of protection from severe illness and hospitalization. The bidirectional relationship between the COVID-19 and liver injury needs to be studied thoroughly as it can severely impact the patient post treatment of the novel Coronavirus disease. Rehabilitative care must be ensured for high risk category or patients shown critical symptoms during the course of treatment. The liver injury induced by the over administration of certain drugs can be easily eliminated by using alternative drugs which is less harmful. As the case fatalities mostly comprised of the comorbid patients, it can easily be controlled by following the COVID-19 appropriate behavior such as wearing masks and not going in crowded places. Vaccinated candidates also should be cautious as the mutations in the virus are rampant. Mutations can some time evade the cover of vaccines.

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