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ICUed COVID-19 Patients with Hepatic Problems during the Third Wave of Coronavirus in Egypt

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Abstract

Background: The pandemic infection of COVID-19 virus is mostly a respiratory infection that has recently begun to harm other vital organs, including the heart, kidney and liver.

Aim of work: The purpose of this study was to investigate the hepatic complications of COVID-19 patients and the risks of being admitted to the ICU or dying.

Methodology: The study included 200 COVID-19 infected Egyptian individuals who had virological symptoms and were tracked until they recovered or died; classified into six parts: co-morbidities (hypertension & diabetes), experienced symptoms of COVID-19, laboratory findings (ALT enzyme level, AST enzyme level, Albumin), complications during hospitalization, treatment protocol used and the survival outcomes.

Results and Conclusion: It was recorded that older people and those with higher blood sugar levels have a higher risk of developing liver-associated COVID-19 disorders. Also, the majority of individuals who developed liver complications in the course of the infection experienced a high mortality rate. Patients with diabetes, hypertension or hepatic disease are at high risk to be admitted into ICU or to die. So, it is important to pay attention to these problems in the diagnosis and treatment of COVID-19 to develop a suitable individualized treatment protocol. There was a correlation between mortality in COVID 19 patients and both high blood sugar levels and high liver enzymes levels. It can be attributed to the diabetes and liver disease correlation as every disease may be the complication to the other, also, COVID 19 can lead to blood sugar level rise in addition to liver enzymes (ALT-AST) levels. Also, there was another suggestion that COVID19 may affect liver and so the chronic liver disease patients.

Keywords: COVID-19; Hepatic problems; third wave

Introduction

Severe acute respiratory syndrome coronavirus 2 (*SARS-CoV-2*) is an RNA virus that was first informed in humans in Wuhan, China, in December 2019. The virus has spread worldwide, triggering the coronavirus 2019 (COVID-19) disease, which continues to have a serious effect on global health [1-4]. The mainstreams of *SARS-CoV-2* patients are asymptomatic or have mild symptoms, such as cough, fever, headache, and anosmia. About 15% have severe pulmonary symptoms for over 10 days, which led to compromised respiration that may convert to failure of multi-organ, coagulopathy, and death. Supplementation with oxygen, invasive ventilation, and other supportive measures are means of the care standard in the hospitalized patients. Still, the mortality percentage remains high amongst patients with some critical diseases. Common risk factors associated with severe COVID-19 are well recognized and comprise advancing age, male sex, and a burden of co-morbidity, as well as hypertension, heart disease, diabetes, and malignancy [5, 6] Lately, there has been some insight into the COVID-19 impact on other organs, as a number of studies have shown that more than half of patients with COVID-19 reported varying levels of liver disease. In addition, a recent study showed that the *SARS-CoV-2* virus might attach to angiotensin-converting enzyme 2 (ACE2) on cholangiocytes, leading to dysfunction of cholangiocyte and inducing a systemic inflammatory response that caused a liver injury. As of March 10, 2020, 7 relatively large-scale hospital-based studies have shown the clinical characteristics of COVID-19 patients, comprise some visions into other factors that provoke COVID-19 induced liver damage. In these studies, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) elevation were informed, ranging from 14% to 53% [7, 8] Moreover, a pathological study of a patient who died from COVID-19 biopsy liver specimens showed moderate micro vesicular steatosis and mild lobular and portal activity, demonstrating that *SARS-CoV-2* could cause liver damage. Though, slight data exists which has comprehensively analysed other enzymes of the liver and clinical characteristics of liver failure amongst patients with COVID-19[9, 10]. In Chinese surveys, one of which was led by Guangzhou Medical University, including 552 hospitals in 31 provincial municipalities during January 2020, many COVID-19 patients had some changes in liver function tests. In particular, 6.2% to 22.2% of patients had elevated AST serum levels, and 21.3% to 28.1% of patients had serum ALT elevated levels, respectively. From 6 studies performed in Wuhan, China, only four included data on the patients' proportion with liver function test results elevation. Specifically, in these four studies, the infected patients' proportion with AST serum

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increase levels ranged from 24.1% to 36.6% [11-13]. In another survey in China, the proportion of patients with AST serum elevation levels was only 16.1%, whereas those with ALT serum elevation levels were not specified. It likely seems that the infected patient's proportion with AST serum increase levels in Wuhan (i.e., the city where the epidemic of COVID-19 began) is much greater than the reported cases outside Wuhan. It is reasonable to speculate that there might have been a higher load of the virus of COVID-19 in patients of Wuhan, where the infection started and was concentrated in a greater of the population percentage [14, 15].

Sex factor in COVID-19 patients-related to dysfunction of liver

A total of 6 case series indicating the abnormal liver function test percentage among patients of COVID-19 proposed that the infected men proportion with AST serum increase levels was higher than infected women. In fact, in these case series, the infected men percentage with AST serum elevation levels were, respectively, 68.7%, 58.2%, 58.1%, 72.4%, 62.8% and 73.2%, whereas the percentage of infected women were, respectively, 31.3%, 41.8%, 41.9%, 27.6%, 37.2% and 26.8%. It can be hypothesized that the infected men are more susceptible to develop COVID-19-related dysfunction of the liver than infected women [16, 17].

The age factor in COVID-19- patients related to dysfunction of liver

Of five case reports also, three were in children, and two were in adults. The children's age ranged from 3 months to 7 years, while the adult age patients ranged from 35 to 56 years. No one of these children had abnormal serum liver enzymes, and consequently, it can be hypothesized that the elderly is related to a higher probability of liver damage/dysfunction [17, 18].

Angiotensin-converting enzyme (ACE) 2-mediated dysfunction of liver

SARS-CoV-2 has direct adverse liver function effects. Some studies have suggested that *SARS-CoV-2* mainly enters alveolar epithelial cells through the ACE2 receptor of humans. Therefore, the lung is supposed to be the main target organ of *SARS-CoV-2* infection [18, 19]. Previous studies have recorded that the epithelial cells of bile duct may also express ACE2 receptors with a proportion 20 times higher than hepatocytes. These reports suggest that *SARS-CoV-2* infection could also lead to cell damage of bile duct epithelial. However, significant elevation of serum alkaline phosphatase level, bilirubin, or gamma-glutamyl transferase (which can reflect bile duct injury) has been rarely indicated in COVID-19 patients. Liver histopathologic features from COVID-19 patients also did not record any significant hepatocytes damage or bile duct cells. So, it is reasonable to assume that COVID-19-related liver dysfunction is more likely because of the secondary liver damage than the use of hepatotoxic therapies or the systemic inflammatory response coexistence, respiratory distress syndrome-induced hypoxia, or multiple organ dysfunction [16-22]. Hence, we decided to do a more detailed study for the infected COVID19 patients focusing on their hepatic state and their treatment protocols.

Patients and methods

The study was conducted on 200 hospitalized COVID-19 patients from Beni-Suef university hospital, Egypt, after the approval of the study by the Research Ethical Committee of the Faculty of Pharmacy, Beni-Suef University (REC-H-PhBSU-20010).

The data were collected from those patients between February and April of 2021. Their data were classified into six parts: co-morbidities (hypertension & diabetes), experienced symptoms of COVID-19, laboratory findings (ALT enzyme level, AST enzyme level, Albumin), complications during hospitalization, treatment protocol used and the survival outcomes.

Results

Specific health parameters and data of 200 Corona virus patients were collected and analysed for more detailed study for the correlation study between the virus infection and the patient health state to specific focus on liver disease patients. Regarding the sex of patients in the study, females were significantly higher than males by double number Figure 1 regarding the age of the patients, only 17% of the patients were between (25-45) years; on the other hand, the majority of the patients were old patients with (60-90) years old that were significantly high in number (Figure 2). The data of the patients showed that, the majority n= (192) of the patients had normal blood pressure level (120/80) and only 8 patients had high blood pressure Figure 3-4 showing, all of the patients had loss of sense of taste and smell as specific diagnostic symptoms for COVID 19 infection. Regarding the patient's health state and symptoms, as Figure 5 showing, 19.9% of the patients had high blood sugar level n= (59), only 11 patients had abdominal pain, 9 patients had diarrhoea, 2 had nausea and only one patient had vomiting. The rest of the patients had no specific symptoms except loss of sense of taste and smell. As Figure 6 showing, only 28% of the patients had higher liver enzymes levels (ALT-AST) that ranged between (90-160) and (60-110) respectively compared with 72% of the patients who had normal liver enzymes levels (7-56) and (10-40) respectively. According to the patient's albumin levels, 50% of the infected patients had 4 g/dl,

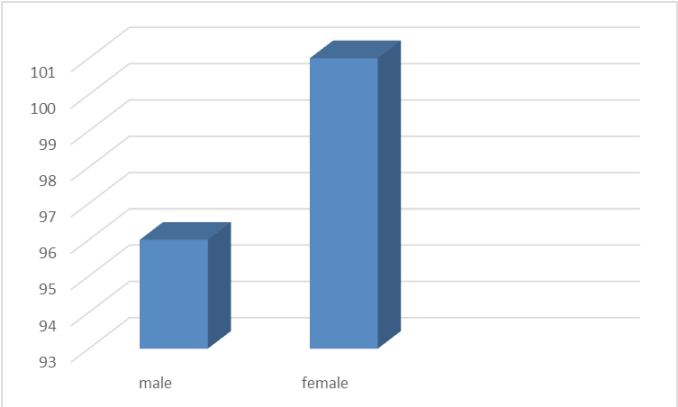

Figure 1: Showing the Covid 19 Patients' Sex.

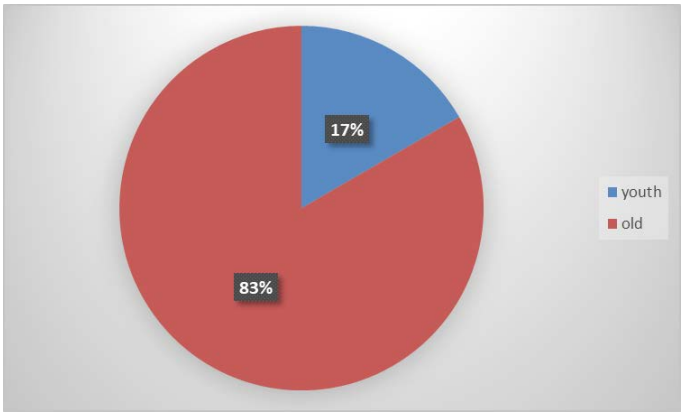

Figure 2: Showing the Covid 19 Patients' Age.

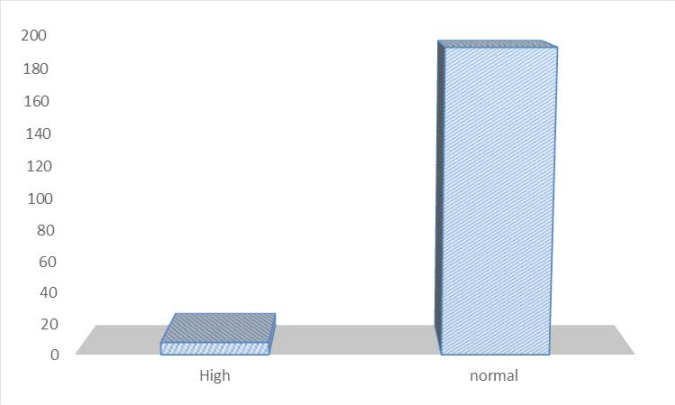

Figure 3: Showing the Covid 19 patients' blood pressure levels.

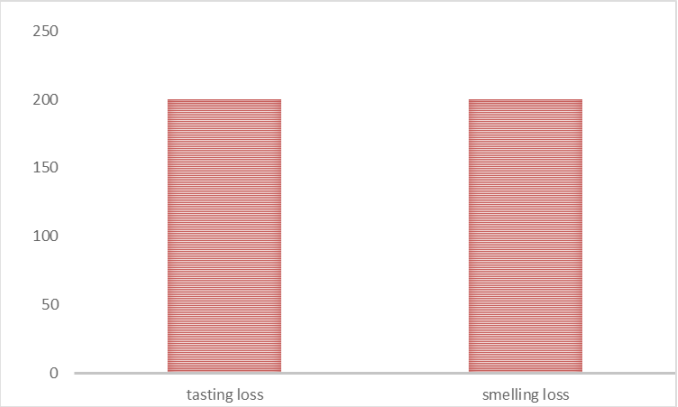

Figure 4: Showing the taste and smell loss of COVID 19 patients.

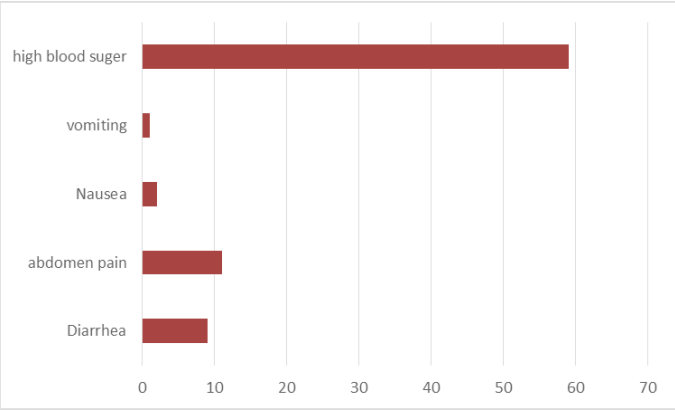

Figure 5: Showing the health state and symptoms of COVID 19 patients.

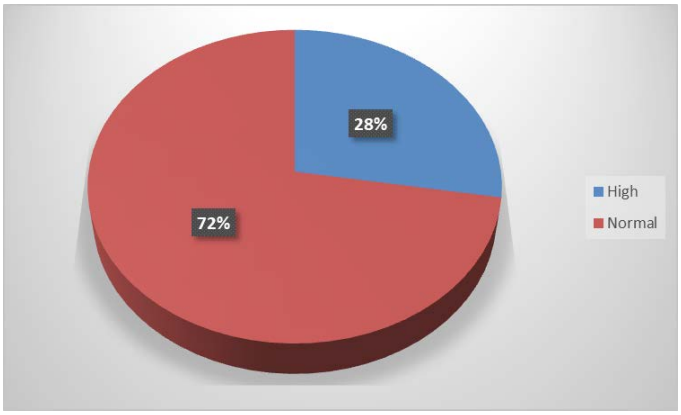

Figure 6: Showing the liver enzymes (ALT-AST) levels of COVID 19 patients.

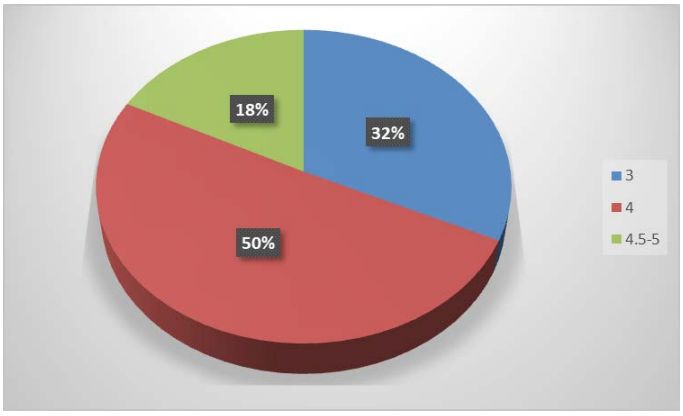

Figure 7: Showing the albumin level of COVID 19 patients.

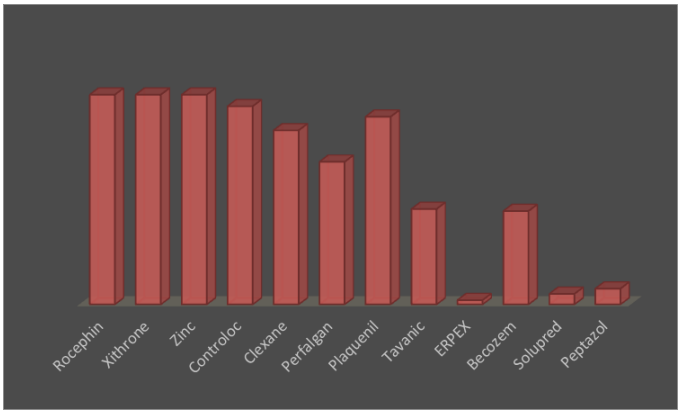

Figure 8: Showing the different treatment protocols for COVID 19 patients.

32 % had 3g/dl and only 18% of the infected patients had (4.5-5) g/dl (Figure 7). According to the treatment protocol in the hospital for 200 COVID 19 patients, all the infected patients had Rocephin, Xithrone and Zinc, on the other hand, 189 patients had Controloc, and 15 had Peptazol. About 166 patients had Clexane, 136 had perfalgan, 179 had Plaquenil, 91 patients had Tavanic, 4 had ERPEX, 89 had Becozem and 10 had Solupred (Figure 8). According to the severity state of the 200 COVID 19 patients, it was recorded that only 10% of the cases needed to be transferred to ICU and the rest of infected patients were normally hospitalized (Figure 9). According to Figure 10 -11 only 3% of COVID 19 patients died, 67% of the dead patients were males and only 33% were females' patients. According to the dead state, it was recorded that 67 % of the dead COVID 19 patients were moved to ICU, and only 33% of the dead infected patients were in hospital normal rooms (Figure 12). According to records reported by Figures (13-15), 67% of the dead COVID 19 patients had high sugar blood levels, high liver enzymes levels (ALT-AST) and normal blood albumin level, on the other hand, 33% of dead infected patients had normal liver enzymes levels, normal sugar blood levels and low albumin level. According to Figure 16, only 17% of the dead COVID19 patients were youth (22-40) and 83% were old patients (55-90) years.

Discussion

The data analysis of our results revealed that, majority of COVID

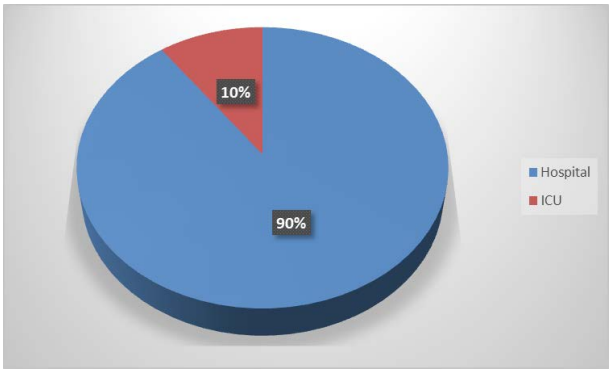

Figure 9: Showing the reservation state of COVID 19 patients.

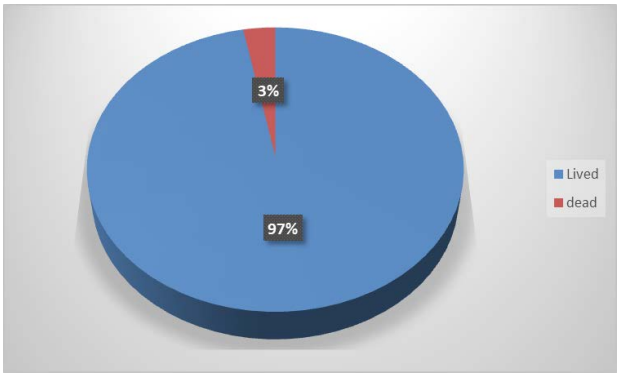

Figure 10: Showing the death percentage among the COVID 19 patients.

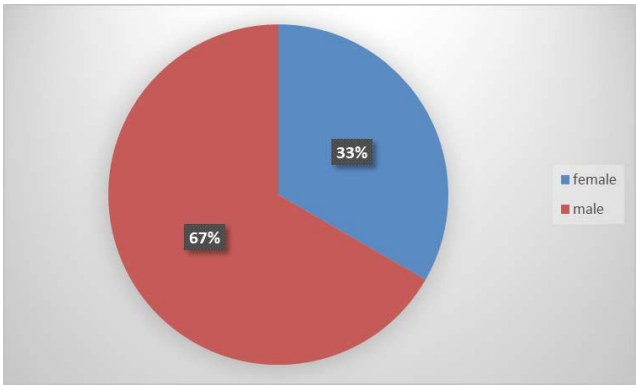

Figure 11: Showing the dead COVID 19 patients' sex.

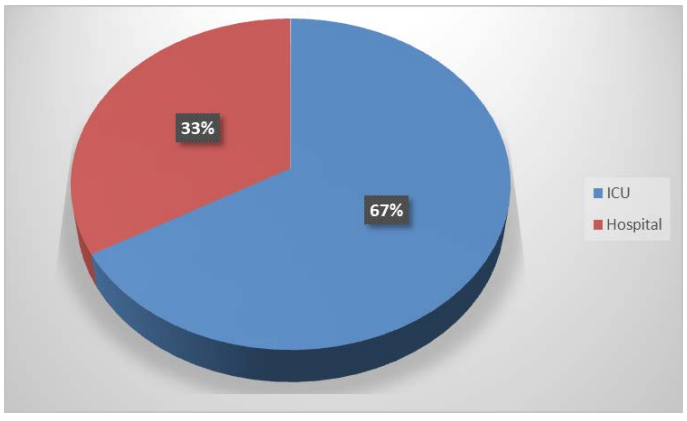

Figure 12: Showing the dead COVID19 patients reserved in ICU.

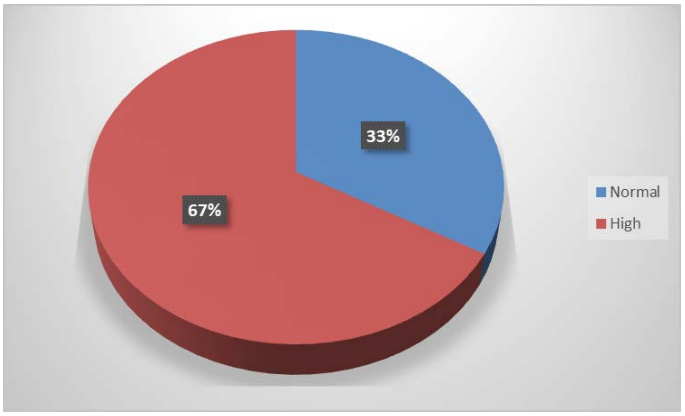

Figure 13: Showing the dead COVID 19 patients' blood sugar level.

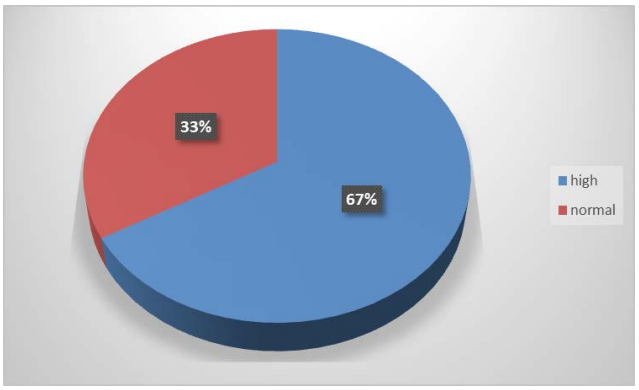

Figure 14: Showing the dead COVID 19 patients' liver enzymes levels (AST-ALT).

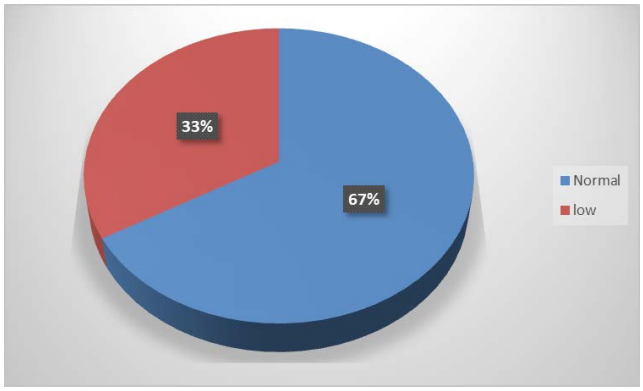

Figure 15: Showing blood albumin level in COVID19 dead patients.

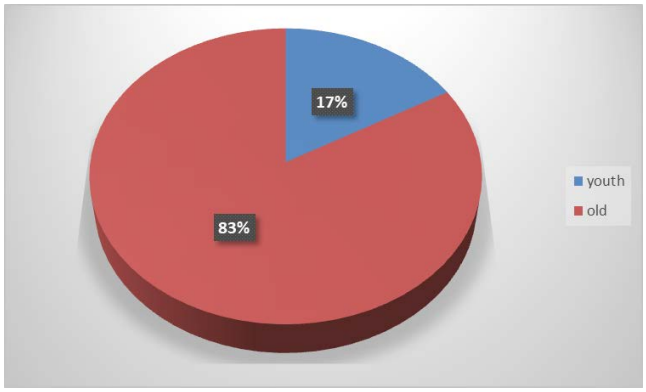

Figure 16: Showing the dead COVID19 patients' age.

19 patients were old men patients. That was shown also in other studies which reported the prevalence of COVID-19 infection found mostly in old males.[23-25] Almost third of patients were suffering from high blood sugar level. Diabetes is considered to be a factor that increase the risk of infection by COVID-19 as it facilitates the viral entry into cell and due to the defect in immune response in diabetic patients.[26, 27] Moreover, they are risky to be ICU admitted. Also, 5% of the patients were hypertensive. A previous study showed that the patients with high blood pressure who infected with COVID-19 had more inflammatory response and higher CRP levels, higher risk of ICU admission, longer hospital stay and longer needing for oxygen therapy compared to non-hypertensive patients [28]. All infected patients in this study had no taste and smell sense as specific symptoms for the COVID-19 infection. It is noticed that loss of taste and smell is a frequent and early symptom for COVID-19[29]. Regarding the liver state of the COVID19 patients, 28% of them showed increase in liver enzyme (ALT-AST) and 32% of them showed decrease in albumin level. These abnormal test results indicate the severity of the patient's cases.[30, 31] The liver injury in COVID-19 patients may be firstly, due to direct coronavirus attack as a reaction to the inflammation cytokine storms of the COVID-19 infection. Secondly, it may be related to side effects of COVID-19 treatment drugs used during hospitalization, which should be evaluated and monitored frequently. Thirdly, some COVID-19 patients who suffer from liver disease may be risky to progress into sever liver injuries. [30, 32] Also, only 10% of the cases needed to be reserved in ICU and the rest of infected patients were normally hospitalized in special rooms. The death percentage of the patients in the study was 3% that was significant high in male old patients who had high blood sugar level and high liver enzyme level and reserved in normal hospital rooms. That indicates that the incidence of liver injury in COVID-19 patients with severe disease is higher than in patients with mild disease. Liver disease is a risk factor, which worsens in patients with COVID-19, and hence it is necessary to pay attention to the occurrence of liver disease in the diagnosis and treatment of COVID-19 to develop effective individualized treatment protocol[33]. We can exclude from these findings that although the laboratory abnormalities in liver function tests are common in COVID-19 patients, the impairment of liver function is not a prominent feature of COVID-19, and also may not have serious clinical consequences. That was reported also in the study of Yafei Zhang [34]. This explain the lower percentage of patients which developed into sever cases who needed ICU admission and the lower mortality.

Conclusion

Patients with diabetes, hypertension or hepatic disease are at high risk to be admitted into ICU or to die. So, it is important to pay attention to these problems in the diagnosis and treatment of COVID-19 to develop a suitable individualized treatment protocol. There was a correlation between mortality in COVID 19 patients and both high blood sugar levels and high liver enzymes levels. It can be attributed to the diabetes and liver disease correlation as every disease may be the complication to the other, also, COVID 19 can lead to blood sugar level rise in addition to liver enzymes (ALT-AST) levels as recorded in many studies [16-22]. Also, there was another suggestion that COVID19 may affect liver and so the chronic liver disease patients [16-22].

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