ASEAN Journal of
Agriculture and Food Engineering

Journal homepage: https://ejournal.bumipublikasinusantara.id/index.php/ajafe

The Association between The Digestive System and Liver Injury in Covid-19 Patients

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ABSTRACT

The increasing number of cases infected with COVID-19 present not only respiratory symptoms but also diarrhea, vomiting, nausea, or abdominal discomfort. Patients who exhibit these symptoms should not be disregarded, and the absence of respiratory manifestations must not rule out COVID-19 infection. We tend to investigate the complications of the digestive system and liver injury for Iraqi patients infected with the COVID-19 virus. We compared the clinical data with two main groups of patients infected. One of them with digestive problems and the other without digestive problems. Several parameters were analyzed: Body Mass Index (BMI), Glutamic Pyruvic Transaminase (GPT), Glutamic-Oxaloacetic Transaminase (GOT), Total Serum Bilirubin (TSB), Anaplastic Lymphoma Kinase (ALK), and Immunoglobulin M (IgM). We classified into several types of patients: G1 (patients without digestive problems who were infected with COVID-19) and G2 (patients with digestive problems while infected with the COVID-19 virus). Each group was compared with two control groups of non-infected individuals. A total of 237 patients were included in the study. The control groups were divided according to obesity by measuring the BMI. The two main groups were compared with two control groups. The study of a patient with different BMI levels shows that most infected patients with high BMI come with gastrointestinal symptoms stronger than respiratory symptoms.

ARTICLE INFO

Article History:
Submitted/Received 01 Oct 2022
First Revised 12 Nov 2022
Accepted 08 Jan 2023
First Available online 08 Jan 2023
Publication Date 01 Mar 2023

Keyword:
Body mass index,
COVID-19,
IgG,
IgM,
Liver enzymes.

1. INTRODUCTION

The current COVID-19 burst of the coronavirus disease is a global emergency; its quick spread and high mortality rate have led to significant consequences. Globally, the number of individuals infected with COVID-19's causative agent, the mild to severe respiratory illness (SARS-CoV2), is quickly increasing. Pneumonia, acute respiratory distress syndrome (ARDS) severe symptoms, and multiple organ failure are all possible in COVID-19 patients (Wong *et al.,* 2020; Ahmed *et al.,* 2021; Kareem *et al.,* 2021; Huang *et al.,* 2020).

An increasing number of studies and clinical observations show that SARS-CoV-2 patients also exhibit diarrhea, vomiting, nausea, and abdominal discomfort in addition to respiratory infection symptoms (Zhou *et al.,* 2020; Abbas *et al.,* 2019; Huang *et al.,* 2020). Not only can gastrointestinal symptoms coexist with COVID-19's characteristic phenotype, but they can also come before it. The patient may experience gastrointestinal manifestations before or after being admitted to the hospital (Song *et al.,* 2020). It's interesting to note that the first COVID-19 case reported in the US had a dry cough as well as a two-day history of nausea and vomiting. The patient experienced loose stools and stomach pain on the second day of hospitalization (Smyk *et al.,* 2020; Al-Bayati *et al.,* 2022). According to the UK analysis, diarrhea affected 13% of the 68 COVID-19 patients (two reported vomiting). These patients' most typical symptoms remained a cough (78%) followed by a sore throat (57%) and fever (40%) (Easom *et al.,* 2020). While the most often reported symptoms of SARSCoV-2 infection in patients are respiratory manifestations like fever and cough, while other organ problems like the GI tract include diarrhea, sickness, and vomiting. Diarrhea, vomiting, and stomach pain were more prevalent in severe COVID-19 patients than in mild COVID-19 patients among GI symptoms (Gu *et al.,* 2020; Kareem *et al.,* 2021).

The prevalence of liver damage in COVID-19 patients was observed ranging from 39.6% to 43.4%, and it was mostly characterized by elevated levels of the enzymes (ALT) and (AST), as well as hypoalbuminemia. In a few patients' total bilirubin (TBIL) levels slightly increased (Chen *et al.,* 2020; Kulkarni *et al.,* 2020). 72 males (54.5%) and 60 females (45.5%) of the 132 COVID-19 cases with liver damage that were found in research by Wang et al. had liver injuries. The age (interquartile range) was 62 years (26–88 years). At the time of admission, the majority of these patients had minor liver damage, with high ALT and/or AST normal levels from 40 to 80 U/L (Ahmed *et al.,*2021; Razooki *et al.,* 1982). Patients with COVID-19 may experience liver complications as a result of medication toxicity and systemic inflammation in addition to liver cell failure, such as the underlying viral hepatitis. Angiotensin-converting enzyme 2 (ACE2), the SARS-CoV-2 receptor, has been discovered to be strongly expressed in both gastrointestinal epithelial cells and the liver, indicating a direct risk of liver damage from SARS-CoV-2. Nearly all of the GI tract's epithelial cells, including those in the stomach, duodenum, small intestine, and rectal area, were shown to express the SARS-CoV-2 virus's nucleocapsid protein and ACE2 protein. ACE2 receptors are extremely abundantly expressed, particularly in the proximal and distal enterocytes (Liang *et al.,* 2020; Xiao *et al.,* 2020).

Many patients infected with COVID-19 are mistreated because the digestive symptoms are much stronger than the repository symptoms. We tend to investigate the intensity of COVID-19 related to the digestive system and the liver. The objective of this study was to help improve the diagnosis of patients. Several parameters were analyzed:

(i) Body Mass Index (BMI)
(ii) Glutamic Pyruvic Transaminase (GPT)
(iii) glutamic-oxaloacetic transaminase (GOT)
(iv) Total Serum Bilirubin (TSB)

DOI:
p- ISSN 2963-9093 e- ISSN 2961-9505

(v) anaplastic lymphoma kinase (ALK)
(vi) Immunoglobulin M (IgM)

2. METHODS

2.1. Patient Collection

The study included a total of 237 individuals that were collected from private clinics and laboratories. All patients attending the doctor clinics are in Baghdad Iraq from Sep. 2021 to Feb. 2022. The average age of these individuals was (20 - 45) years. The study group includes 127 males and 110 females. The patients were divided into four main groups the first is control with no previous infection of COVID-19 and without any digestive problems having normal BMI (CND=63). The second group is patients infected and who do not suffer from digestive problems during the infection (ND=65). The third group is patients with digestive problems during the inflation of COVID-19 we shall call it (D=52). The fourth group is the control group with no previous infection of COVID-19 with high BMI shall be named (CD=57). **Figure 1** describes the distribution of the groups.

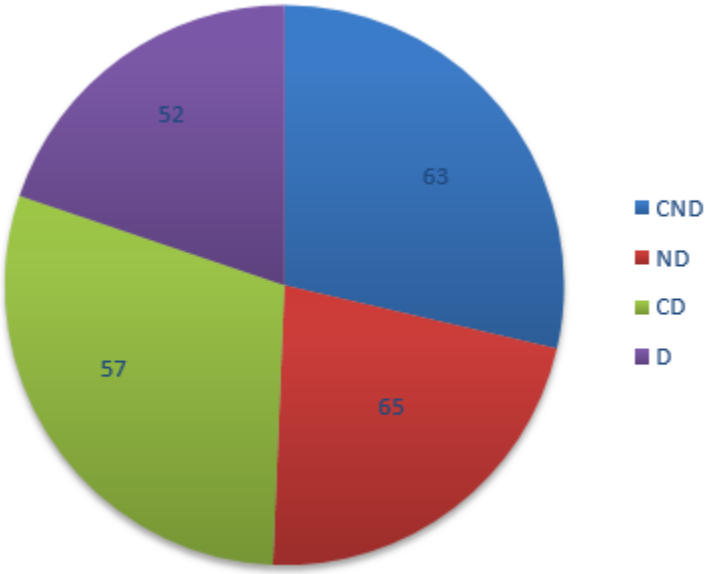

Figure 1. Groups included in the study.

2.2. Sample collection

Venous blood (5-10mL) was taken from each patient. The blood was divided into EDTA tubes for CBC and serum jell tubes were left at 37 ºC temperature and then separated by centrifugation at (4000xg) for 5 minutes. The obtained serum was stored at (-20) ºC until being used for different investigations.

2.3. Laboratory test.

Covid-19 antibody (IgG and IgM) was measured by using the commercially available (Boditech Med. Inc. Korea). All procedures were carried out according to the manufacturer's instructions. The liver enzyme (AST, ALT, TSB, and ALK) using the spectrophotometric method by a commercially known company named (HUMAN, Germany) (Vollet-Filho *et al.*, 2022).

DOI:
p- ISSN 2963-9093 e- ISSN 2961-9505

2.4. Statistical Analysis

Data were statistically analyzed by SPSS software version 22. The variables were reported as means ± standard deviation. The groups were compared by using one-way ANOVA and post hoc Tukey test, with a P value of <0.05 indicating the statistically significant difference.

3. RESULTS AND DISCUSSION

The results are presented in **Table 1**. As we recorded the information (Vomit, Diarrhea, Abdomen pain) that was gathered in our study we found that patients with high BMI were most likely to have digestive problems and gastrointestinal complications, as well as liver disorder. **Table 1** shows the relationship between the liver enzyme and BMI for covid-19 patients.

Table 1. Relationship between the liver enzyme and BMI for covid-19 patients.

P-Value		Patient ND	Patient D	Control ND	Control D	Parameters
1.000	CDand D	0.010 ±0.000	0.010 ±0.000	0.010 ±0.000	0.010	IgG
1.000	CNDand ND				±.0000	
1.000	Dand ND					
0.000	CDand D	1.642±.0.863	1.253 ±0.537	0.010 ±0.000	0.010	IgM
0.000	CNDand ND				±0.000	
0.006	Dand ND					
0.285	CDand D	19.650	24.870±1.695	19.727 ± 1.529	25.496±0.	BMI
0.996	CNDand ND	±1.487			969	
0.000	Dand ND					
0.047	CDand D	18.686±4.330	35.441±3.390	20.813±10.517	29.859±14	GPT
0.667	CNDand ND				.199	
0.000	Dand ND					
0.003	CDand D	13.727	30.944±3.264	17.039 ±8.506	24.836	GOT
0.231	CNDand ND	±4.481			±11.261	
0.000	Dand ND					
0.000	CDand D	0.565±0.331	1.031 ±0.202	0.64±0.195	0.689±0.2	TSB
0.008	CNDand ND				11	
0.000	Dand ND					
0.000	CDand D	63.213±22.36	143.947±24.305	93.842±7.670	96.923±17	ALK
0.279	CNDand ND	7			.428	
0.000	Dand ND					

After measuring the variable above for the healthy individuals and patients we exhibit the following measurements.

The AST, ALT, ALK, and TSB showed highly significant towered the BMI p = 0.00, 0.00, 0.00, 0.01 in comparison with the control group for the high BMI patients.

DOI:
p- ISSN 2963-9093 e- ISSN 2961-9505

The patient with a normal BMI displayed no elevation in the liver enzymes. As we recorded the digestive complications for low BMI patients with covid-19 we found the number of patients who had digestive problem symptoms is fewer than the patient with high BMI.

The liver enzymes showed a high positive correlation towards the BMI for patients infected with COVID-19 **(Table 2)**. This indicates that obesity is a major factor in showing digestive symptoms and liver enzyme elevation.

Table 2. Correlation of group G1 N=63 patients with digestive problems.

P	Pearson correlation	Parameters
0.000	1.000 *	BMI and GPT
0.000	0.880*	BMI and GOT
0.000	0.552*	BMI and TSB
0.143	0.248	BMI and ALK
0.737	-0.056	BMI and IgM

* Correlation is significant at the 0.05 level

The correlation of the normal BMI group shows poor positive significance towered the liver enzymes. This lead to conclude that BMI or obesity is a major fact of digestive problem during the COVID-19 infection **(Table 3)**.

Table 3. Correlation of group G2 N=50 patients without digestive problems.

P	Pearson correlation	Parameters
0.295	-0.174	BMI and GPT
0.295	-0.174	BMI and GOT
0.742	-0.055	BMI and TSB
0.070	0.297	BMI and ALK
0.958	0.009	BMI and IgM

* Correlation is significant at the 0.05 level

Healthcare workers who have SARS-CoV-2 infections can also experience gastrointestinal symptoms, according to a retrospective investigation of 54 infected medical staff members from one hospital in Wuhan (Chen *et al.,* 2020). Nine patients who were admitted with merely gastrointestinal symptoms saw five of them develop classic COVID-19 symptoms within two to five days, while the other four remained symptom-free throughout their hospital stay. More than half of SARS-CoV-2-positive patients were admitted to the gastrointestinal department as a result of the early symptoms (such as nausea, vomiting, and diarrhea). Previous SARS investigations provided evidence that coronavirus has a gastrointestinal tract tropism. Patients with SARS could easily find the SARS-CoV RNA in feces samples.

No studies on the relationship between BMI and digestive symptoms of COVID-19 patients. Much research has been done regarding liver and kidney injury but not related to BMI. Recent studies on COVID-19 have shown in COVID-19 patients, the incidence of increased liver aminotransferases varies from 2.5% - 76.3%. The pooled incidence for AST and

DOI:
p- ISSN 2963-9093 e- ISSN 2961-9505

ALT levels outside the normal ranges was 20%-22.5% and 14.6%-20.1%, respectively, in a recent meta-analysis (Wang *et al.,* 2020). In up to 35% of cases, these abnormalities are accompanied by mildly elevated total bilirubin levels. While increases in cholestatic liver enzymes (ALP) were previously thought to be uncommon, new systemic reviews show ALP elevation in 21.1% of COVID-19 patients, respectively. Although SARS-COV-2-related liver injury has been observed to be mild, it may impact a significant percentage of patients, particularly those having a more chronic disease course.

An earlier Pakistani study of obese patients without COVID-19 agreed with our study, A number of the gastrointestinal manifestations investigated were more common in the overweight patient. Obese people are also more likely to acquire gastrointestinal problems (Ahmed *et al.,* 2020). Another study supports our study done by the University of Campus Bio-Medico di Roma on patients without COVID-19. An increasing amount of research confirms the link between obesity and an increased chance of developing digestive problems. Obesity not only raises the chance of having gastrointestinal diseases but it is also linked to more serious disease symptoms and a reduced response to treatments, resulting in more unfavorable clinical outcomes in general, with a corresponding clinical and economic burden

4. CONCLUSION

In our study, we discover a strong relationship between obesity and the elevation of liver enzymes while developing gastrointestinal symptoms. The outcome of our study is that patients are mistreated if the digestive symptoms are stronger than the respiratory symptoms. Patients with these symptoms should not be overlooked, and the SARS-CoV-2 infection should not be ruled out in the absence of respiratory symptoms.

5. ACKNOWLEDGMENT

We would like to express our gratitude to all staff of the Hydrogen Medical lab., Calcium Medial lab, and Nursing privet Hospital. We sincerely thank the patients and healthy people who supplied us with blood samples.

6. AUTHORS' NOTE

The authors declare that there is no conflict of interest regarding the publication of this article. Authors confirmed that the paper was free of plagiarism.

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p- ISSN 2963-9093 e- ISSN 2961-9505

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DOI:
p- ISSN 2963-9093 e- ISSN 2961-9505