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Research Article
Evaluation of Markers of Liver Damage in Patients Infected with SARS-CoV2

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Abstract

Background and Objective: SARS-CoV-2 infection is the cause of many complications that can affect many organs, hepatic manifestations have been described due to the existence of hepatic tropism. The objective of this study was to assess the markers of liver damage in patients infected with SARS-CoV-2 monitored at the epidemiological treatment centre of fann. **Materials and Methods:** This is a prospective analytical study. Were included 202 subjects infected with SARS-CoV-2. The parameters studied were on the one hand age and sex and on the other hand transaminases (ALT, AST), GGT (gamma GT), PAL (alkaline phosphatase), serum albumin, total and direct bilirubin. Parameter assays were performed with the A15 Chemistry Analyzer. The statistical test used for data processing is the Chi. A $p<0.05$ was considered significant. **Results:** The average age was 60 years with a sex ratio of 1.12. The analysis of the biological parameters in the patients shows an increase in the activity of the hepatic enzymes in 38.12 and 48.02% of the patients, respectively for ALT and AST. PAL and GGT activity was increased, respectively in 25.25 and 61.88% of patients. Hypoalbuminemia was found in 61.88% of patients and an increase in total and direct bilirubin, respectively in 14.36 and 39.60% of patients. The analysis of the results according to the syndrome markers had shown in the patient's frequencies of 44, 28 and 18%, respectively for cholestasis, cytolysis and mixed damage. **Conclusion:** Liver disturbances could be used as markers to dictate the prognosis of COVID-19 severity.

Keywords: Covid-19, tropism, SARS-CoV-2, syndrome markers, liver damage, prognosis, epidemiological treatment centre

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The coronavirus family is responsible for respiratory infections in mammals and birds. These are RNA viruses, grouped into four subfamilies, two of which are responsible for severe and potentially fatal pathologies: SARS-CoV-1 and MERS-CoV, identified, respectively in 2003 and 2012[1]. In December, 2019, the appearance of several cases of pneumonia of unknown origin in the province of Hubei in China, led to the identification, in January, 2020, of a new coronavirus, called SARS-CoV-2 by the group Coronavirus Working Group of the International Committee on Taxonomy of Viruses. SARS-CoV-2 causes a sometimes severe respiratory disease, named COVID-19 by the World Health Organization[2]. Covid-19 is associated with many biological complications affecting many organs and tissues due to their expression of the ACE2 receptor[3,4]. First known by its clinical manifestations such as fever and respiratory symptoms, COVID-19 disease can be revealed by extra-pulmonary signs, including gastrointestinal and hepatic manifestations raising the potential tropism of SARS-CoV-2 for the digestive tract, numerous studies show that liver disturbances are common in patients with COVID-19, which should be of concern[2,5]. Thus, the objective of this work was to evaluate the markers of liver damage in patients infected with SARS-CoV-2 followed at the Epidemiological Treatment Centre of the National University Hospital of Fann.

MATERIALS AND METHODS

This was a prospective analytical study carried out during the period from June-September, 2021. The patients recruited were followed at the level of the infectiology Departments of the epidemiological treatment centre and in whom the diagnosis of COVID-19 was confirmed by RT-PCR, the study did not concern suspected patients with a negative RT-PCR and patients with a history of liver damage. Blood samples were taken from the subjects by venipuncture at the elbow crease with a tourniquet. The blood was collected in a dry tube centrifuged at 3500 rpm for 5 min. Biochemical parameter assays were performed with the A15 Chemistry Analyzer, BioSystems (Spain, Barcelona). In this study, liver damage was classified according to syndrome markers in cytolysis, cholestasis or mixed damage:

- Cytolysis if ALT and/or AST $\geq 2\times$ upper limit of normal (ULN)
- Cholestasis if PAL and/or GGT and BILT (total bilirubin) or BILD (direct bilirubin) $\geq 2\times$ ULN
- Mixed if the combination of ALAT and/or ASAT $\geq 2\times$ LSN and PAL and/or GGT and BILT or BILD $\geq 2\times$ ULN

The recording of the data and the exploitation of the results were made by the Excel 2016 software, which had allowed us to calculate the descriptive data. The statistical test used for data processing is the Chi-square test, this test was performed by the GraphPad Prism 8.0.2 software (GraphPad Software Inc, San Diego, CA, USA). A $p<0.05$ was considered significant.

RESULTS

The current study population consisted of 202 subjects with COVID-19. The average age of our subjects was 60 years old with extremes of 23 and 96 years old. The sex ratio was 1.12. Liver test abnormalities were defined according to the standards of the reference interval of the laboratory in Fann: ALT >41, AST >40, PAL >270, GGT: Man >86 and Woman >48 IU L^{-1}, BILT >1 mg dL^{-1}, BILD >0.25 mg dL^{-1} and Albumin <38 g L^{-1}. As part of our study, we considered abnormal liver function tests if at least one of the liver parameters studied was above the upper limit of normal (ULN) mentioned above. The analysis of the distribution of the results showed a disturbance of the liver balance sheet in 67.33% of the patients while 32.67% had a normal liver balance sheet (Fig. 1).

The distribution of hepatic abnormalities according to age groups shows a prevalence of 86.36% of disturbances in liver function tests in the age group (77-96 years) (Fig. 2).

Analysis of the distribution of hepatic abnormalities by sex showed a male predominance (74.77%) against 58.95% in women (Fig. 3).

The determination of the averages of the biochemical parameters studied in the patients showed enzymatic activities of the order of 47.56, 52.81, 209.4 and 111.5 UI L^{-1}, respectively for ALT, AST, PAL and GGT. Levels of 0.71, 0.25 mg dL^{-1} and 36.43 g L^{-1} were found for BILT, BILD and albumin, respectively (Table 1).

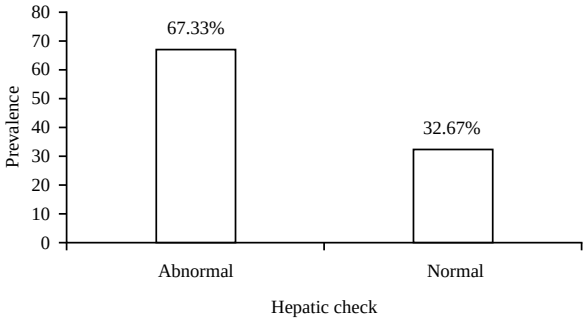

Fig. 1: Distribution of patients according to the presence or absence of liver abnormalities
$p<0.05$

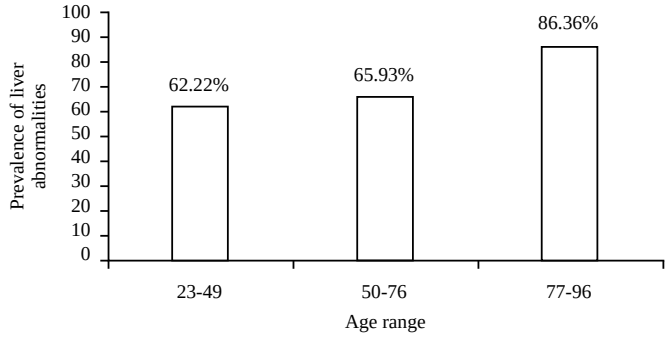

Fig. 2: Frequency of liver abnormalities by age

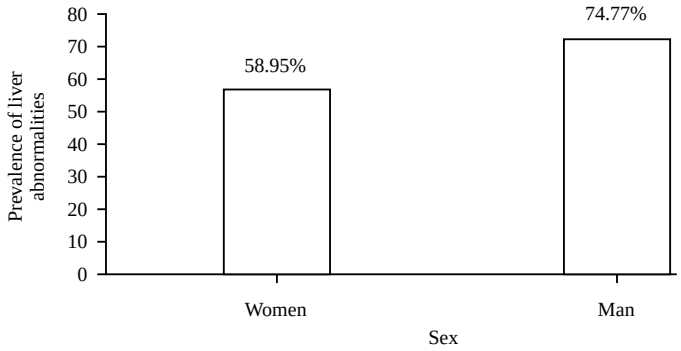

Fig. 3: Frequency of liver abnormalities by sex

p = 0.039

Table 1: Means of biological parameters in our study population

	Minimum	Average	Maximum	Common values
ALT	12	47.56	385	<41 IU L^{-1}
AST	11	52.81	340	<40 IU L^{-1}
PAL	65	209.4	704	98-270 IU L^{-1}
GGT	19	111.5	474	M: 16-86 IU L^{-1}
				W: 12-48 IU L^{-1}
BILT	0.15	0.71	6.62	<1 mg dL^{-1}
BILD	0.01	0.25	1.26	<0.25 mg dL^{-1}
Albumin	5.09	36.43	50.71	38-44 g L^{-1}

Table 2: Distribution of disturbances according to the type of liver damage according to age and sex

		Frequency according to gender (%)		Frequency by age (%)	
Disturbances	Frequency in the population (%)	H	F	<50 years old	>50 years
Cytolysis	28	65.79	34.21	21.05	78.95
Cholestasis	44	41.67	58.33	18.33	81.67
Mixed damage	18	64	36	28	72

The analysis of the distribution of the parameters showed increased enzymatic activities of ALAT, ASAT, PAL and GGT, respectively in 38.12, 48.02, 25.25 and 61.88% of the patients. An increase in total and direct bilirubin levels was observed, respectively in 14.36 and 39.60% of patients and a decrease in albumin in 61.88% of patients. (Fig. 4).

Analysis of the results showed frequencies of 44, 28 and 18%, respectively for cholestasis, cytolysis and mixed damage. Breaking down the type of liver damage by gender, 65.79% of men had cytolysis and 58.33% of women presented with cholestasis syndrome. Analysis of the results according to age showed a predominance of hepatic disturbances in subjects over 50 years of age (Table 2).

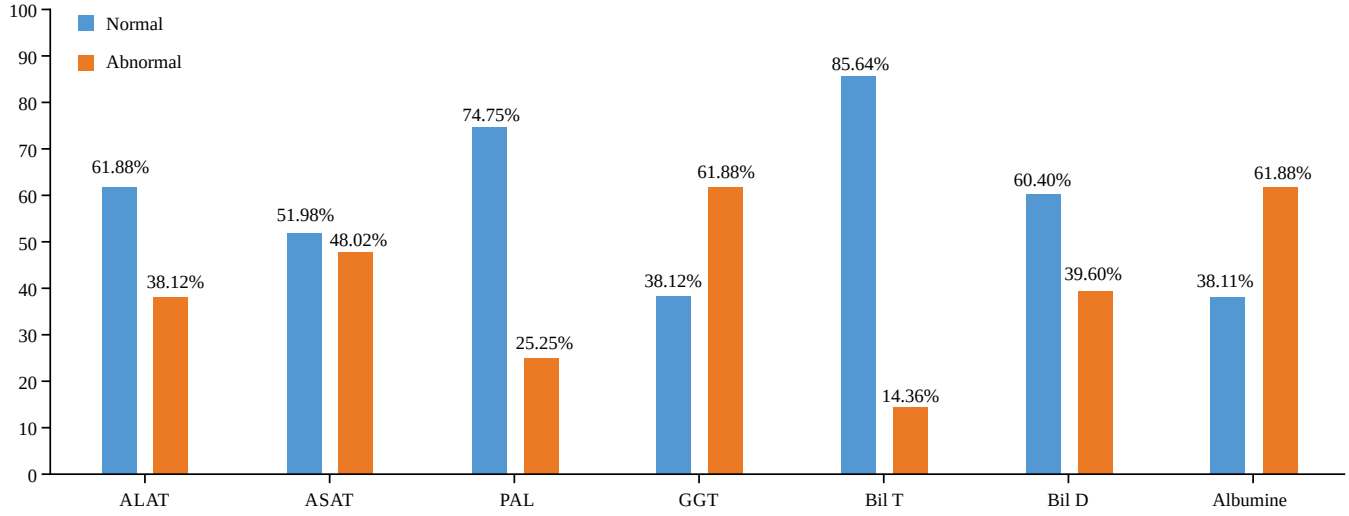

Fig. 4: Distribution of the biological parameters studied in our study population according to the reference values

DISCUSSION

SARS-CoV-2 infection, called COVID-19, causes life-threatening pneumonia[6]. Additionally, there is a growing body of literature showing that liver damage is common in patients with COVID-19, which should be of concern[7,8]. It is in this context that we have set ourselves the objective of evaluating markers of liver damage in patients with COVID 19. The exploitation of these results made it possible to show that the average age of our population was 60 years, with extremes of 23 and 96 years and a sex ratio of 1.12. The predominance of the male sex in patients infected with SARS-CoV-2 has already been reported by several studies such as Hwaiz *et al.*[9], Xu *et al.*[10], this may be linked to a higher expression of the ACE2 receptor in men compared to women[11]. Other studies have attributed it to the hormonal difference indeed female sex hormones (estrogen, progesterone) have an anti-inflammatory role and influence immune cells (production of antibodies)[12]. Evaluation of biochemical parameters in our population showed averages of 47.56, 52.81, 209.4 and 111.5 UI L^{-1}, respectively for ALT, AST, PAL and GGT. The means obtained for BILT, BILD and albumin were, respectively 0.71 and 0.25 mg dL^{-1} and 36.43 g L^{-1}. Altaf *et al.*[13] in a study conducted in Pakistan had found higher averages[10]. Analysis of the distribution of parameters showed an increase in liver enzyme activity in 38.12 and 48.02% of patients respectively for ALAT and ASAT. PAL and GGT activity was increased, respectively in 25.25 and 61.88% of patients. Hypoalbuminemia was found in 61.88% of patients and an increase in total and direct bilirubin respectively in 14.36 and 39.60% of patients. The frequencies found in this work were higher than those obtained by Fan *et al.*[14] and Hundt *et al.*[15], however, the frequencies obtained for transaminases and PAL in our study were close to those obtained in Iraq by Hwaiz *et al.*[9] and Kumar *et al.*[16] had found in a meta-analysis frequency for total bilirubin and albumin similar to our results. Many factors can lead to impaired liver function tests during COVID-19 including immune-mediated inflammatory response, drug-induced liver injury, hepatic congestion and direct viral toxicity[17]. A significant increase in liver enzyme activities in men (74.77%) compared to women (58.95%) was observed. Moreover, there was a direct positive correlation between these hepatic enzyme disturbances with age ($p<0.05$), this result was similar to that of Saini *et al.*[18]. Analysis of the results according to the type of liver damage showed frequencies of 44, 28 and 18%, respectively for cholestasis, cytolysis and mixed damage. In a study carried out in India frequencies of 53.48, 27.9 and 18.6%, respectively for cytolysis, cholestasis and mixed involvement were found[18]. The results obtained were following the literature, in fact, the angiotensin-2 converting enzyme receptor, which is the target of SARS-CoV-2, is strongly expressed in the epithelial cells of the bile ducts[19]. Breaking down by sex, no significant difference was found in the incidence of a type of liver injury in men and women ($p>0.05$). Analysis of the results by age showed a predominance of hepatic abnormalities in subjects over 50 years old ($p<0.05$). The underlying reason for liver injury during COVID-19 is still unclear and several mechanisms are discussed in the literature[20]. These mechanisms are related to direct cytotoxicity resulting from active viral replication in

liver cells expressing the receptor ACE2[21]. Other hypotheses are mentioned, in particular the reactivation of pre-existing liver disease but also patients with pre-existing chronic liver disease are predisposed to liver damage induced by SARS-CoV-2 infection[22]. A cause of drug origin has been reported, indeed the acetaminophen (antipyretic) used in the therapeutic management of patients with COVID-19 could cause liver damage[22] but also other substances such as oseltamivir, abidol or lopinavir, may have hepatotoxic effects[23].

CONCLUSION

The current study showed the existence of liver damage in patients with COVID-19. The degree of liver damage reflects the severity and increased mortality, liver disturbances could be used as markers to dictate the prognosis of the severity of COVID-19. However, it might be better to test the effect of drugs and the duration of drug administration on liver enzyme activities. further studies are needed to better explore the mechanisms of COVID-19-induced liver injury.

SIGNIFICANT STATEMENT

The COVID-19 pandemic has caused many deaths with an impact on the global economy, this study is part of the proper management of patients infected with SARS-CoV-2 and the response to the pandemic. Our experience feedback in the management of the COVID-19 pandemic has shown the existence of liver lesions in patients infected with SARS-CoV-2. These disturbances can be used in the evaluation of the prognosis and ensure better patient care.

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