Original Article

A Retrospective Analysis of Hematological Parameters' Comparison Before and After COVID–19 Exposure

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Abstract

Coronavirus Disease 19 was identified to cause severe pneumonia and multisystemic complication including gastrointestinal, and central nervous system. Changes in hematological parameters were reported in several studies among patients affected by SARS-CoV-2 in different countries. Significant liver enzymes elevation in alanine aminotransferase (ALT), aspartate aminotransferase (AST) occurred in a good percentage of patients specially more in sever than mild/moderate COVID-19 patients. Our retrospective study aimed to evaluate the hematological parameters with special emphases on hemoglobin (Hb), ALT, AST, and alkaline phosphatase (ALP) levels in 77 Saudi patients, comparing their levels before and after COVID-19 exposure. The main findings revealed a significant drop in hemoglobin level (p=0.015), while showed a significant elevation in both ALT (p=0.001) and AST (p=0.0001), while significant decrease in ALP (p= 0.016). The platelets, PTT, and creatinine values were statistically insignificant with p value above 0.05. These observations on Saudi patients suggested that a routine liver function test should be performed to monitor liver function and prognosis after recovery.

Keywords: Coronavirus, COVID-19, Liver Injury, Hematological Parameters.

Introduction

Coronavirus Disease-19 (COVID-19) was first identified to cause **S**evere **A**cute **R**espiratory **S**yndrome **Co**rona **V**irus-**2** (SARS-CoV-2), being pandemic and a major health crisis in the past three years. The virus structured as an enveloped non-segmented positive sense RNA virus; originated from beta-coronaviruses. High percentage of similarity was reported between SARS-CoV-1 (2003 pandemic) and current SARS-CoV-2; both belonging to beta-coronaviruses family.[1] In Saudi

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Arabia as of 3 May 2023 a total of 840,337 confirmed cases, including 9,643 deaths from COVID-19, reported by World Health Organization.[2] The coronaviruses known to cause a multisystemic infection of respiratory, gastrointestinal, and nervous system in human and other mammalians. Beside respiratory complications, gastrointestinal symptoms were observed including nausea, loss of taste, vomiting, and diarrhea. Several studies reported positive tests of COVID-19 using anal swap specimen from infected patients, pointing to the possible of COVID-19 fecal oral transmission.[3] Few bioinformatic studies reported the Angiotensin Converting Enzyme 2 (ACE2) found on surface of alveolar cells and on intestinal epithelium cells, is serving as a COVID-19 route of infection. Therefore, there is a strong association between digestive system complications and COVID-19 infection.[3] COVID-19 was reported to cause a liver injury with elevated liver enzymes levels.[4] Liver injury in patients affected with COVID-19 ranges from mild and temporary to severe leading to liver frailer, taking in consideration the presence of previous chronic liver complication; needed to be taken inconsideration during disease management.[5] Liver enzyme elevation ranges from 15% to 58% in those patients.[6,7] The liver damage pathogenesis is not fully defined, being currently under investigation.[5]

In Saudi Arabia, liver enzymes elevation due to the exposure to COVID-19 has not been reported yet. This study aimed to confirm the association between SARS-CoV-2 infection and the changes in hematological parameters with special emphases on hemoglobin (Hb), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) levels comparing their levels before and during COVID-19 exposure. The elevation in liver enzymes should be taken in consideration while monitoring the prognosis of COVID-19 complication specially in severe cases.

Methods

Study Population

The study was conducted at King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia. A retrospective study on 77 Saudi COVID-19 patients between January 2020 to June 2021.

Inclusion Criteria

Participants aged between 12 - 81 years, COVID-19 positive confirmed by rRT-PCR from the 7th January 2020 to 15th June 2021. Hematological parameters were examined before and during COVID-19 infection.

Exclusion Criteria

Patients with no hematological parameters results before and during COVID-19 exposure.

Patients with previous hepatic complications.

Demographic Data

The demographic information of the 77 participants in the study included both male and female from Saudi Arabia. The data are summarized in Table 1.

Data Collection

Patients' clinical data were retrospectively extracted from the patients' clinical records. Since it is a pandemic, we have over 30,000 patients file records were screened. Only patients with required hematological parameters results before and during COVID 19 exposure were selected. Data included age, date of diagnosis, type of test, other diseases, COVID-19 symptoms, WBCs count, RBCs count, Platelets Count, Hemoglobin level, PTT level, ALT level, AST level, ALP level, and Creatinine level.

Data Analysis

SPSS (Statistical Package for the Social Sciences v21.00) was used for analyzing the percentage (frequency) and describing the categorical variable. Comparisons of the analyte levels between the value before and during COVID-19 were performed using independent t test and Mann Whitney U test. Differences between the values before and during COVID-19 were considered statistically significant with p value less than 0.05.

Results

Table 1 summarize demographic features of patients involved in the study. 77 patients were included in the study, 58% were males and 42% were females. The Inter Quartile Range median (IQR) age of subjects was 58 (46, 70) years. About 90% of the subjects had symptoms on arrival: 68% with cough, 63% with fever, 45% with shortness of breath, and only 14% with sore throat. 31% of the patients were from home isolation, 21% from wards and 7% from the ICU. Severity of cases were only in 6% of cases, while 21% were moderate and 73% were mild. Patients in this study have health complications: hypertension complication (54%), diabetes (48%), and dyslipidemia (31%), while 16% have no complications.

Table 1: Demographic Features of study subjects (n=77).

Variable	Frequency (%)
Age in years, Mean (± SD)**	58 (±18)
Gender	
Male	44 (58 %)
Female	33(42%)
Symptoms on arrival	
Cough	53 (68%)
Fever	49 (63%)
Shortness in breath	35 (45%)
Sore throat	11 (14%)
Patient Status	
Home Isolation	24 (31%)
ICU	5 (7%)
Ward	16 (21%)
Not mentioned	32 (41%)
Severity of COVID cases	
Mild	56 (73%)
Moderate	16 (21%)
Severe	5 (6%)
Complications (Present* n=65)	
-Hypertension	35 (54%)
-Diabetes	31 (48%)
-Dyslipidemia	20 (31%)
No complication	12 (16%)

*Subjects can have more than one complication
**SD: Standard Deviation

Table 2 summarize the hematological parameters of study subjects before and during COVID 19. The hematological parameters before and during COVID 19 of subjects were compared using statistical tests namely independent t test and Mann Whitney U test for data distribution. The Hemoglobin mean value was statically different during than before the exposure (p= 0.010). ALT and AST showed similar significant elevation during exposure than before (p=0.001), while ALP showed significant decrease during exposure (p=0.016). The platelets, PTT, and creatinine values were statistically insignificant with p value > 0.05.

Table 2: Hematological Parameters Comparison the of Samples of COVID 19 Patients before and during COVID 19 Exposure.

Hematological Parameters	Samples out of 77(%)	Normal Range	Before COVID 19 Exposure Descriptive Statistics [a]	During COVID 19 Exposure Descriptive Statistics [a]	*p* value
WBC	70 (91%)	4 - 11×10^9/L	7.32 ± 2.57	6.43 ± 3.91	0.082
Hemoglobin	68 (88%)	120 – 160 g/L	126.79 ± 19.31	123.46 ± 20.88	**0.015***
Platelet	70 (91%)	150 - 400× 10^9/L	258.5 (203.7, 302)	240(201, 338.5)	0.543
PTT	24 (31%)	25-35 sec	28.6(26.28, 32.35)	28.85(26.38, 31.7)	0.225
ALT	61(79%)	5 -55 U/L	16(1.5, 24)	25(14.5, 43.5)	**0.001***
AST	60 (78%)	5 - 34 U/L	18(5, 25)	31(20.25, 48)	**0.001***
ALP	48 (62%)	40-150 U/L	85(68, 97)	76(64, 91)	**0.016***
Creatinine	70 (91%)	50 -98 µmol/L	99.69 ± 74.08	90.09 ± 67.49	0.169

*Statistically significant at 5%
[a] Mean and SD was used for Normally distributed data; Median and IQR used for skewed data.

The results in table 3 showed a comparison between genders and their hematological parameters during COVID 19 exposure. The result showed a significant decrease in hemoglobin levels in female compared to male during exposure of COVID-19 (p=0.007). ALT levels in table 2 showed to be elevated in general during exposure. Table 3 showed a significant difference in ALT values in men (28) compared to women (20) (p=0.037). Thus, the results indicate a significant decrease in hemoglobin in women compared to men during CIVID 19 exposure, while ALT elevated more in men than in women.

Table 3: Hematological Parameters Comparison the of Samples of COVID 19 Patients-based on Gender.

Hematological Parameters	Normal Ranges	Gender		*p* value
		Male (n=45)	Female (n=33)	
		Descriptive Statistics [a]		
WBC	4 - 11×10^9/L	6.34 ± 3.79	6.33 ± 3.95	0.990
Hemoglobin	120 – 160 g/L	130.52 ±19.83	117.5 ±20.35	**0.007***
Platelets	150- 400× 10^9/L	247(190.5, 393.5)	235.5(211.75, 288)	0.382
PTT	25-35 sec	28.8(26.3, 31.7)	29.2(26.4, 32.5)	0.971
ALT	5 -55 U/L	28(16, 47)	20(12.5, 35.75)	**0.037***
AST	5 - 34 U/L	33.5(22.5, 51)	27(17.25, 46)	0.135
ALP	40-150 U/L	76(65.5, 90)	76(50.75, 93.25)	0.668
Creatinine	50 -98 µmol/L	88.64 ± 53.70	91.56 ± 79.02	0.848

Discussion

COVID-19 caused by SARS-CoV-2 virus as mentioned earlier a multisystem infection. Several studies reported digestive complications along with respiratory dysfunction. COVID-19 highly affect liver function, causing higher mortality and morbidity by losing liver cells viability. Hepatocellular or liver cell damage/ injury reflected usually by showing an elevation in ALT and or AST with normal ALP levels. Biliary injuries reflect more elevation in ALP. Those observation has been reported in the literature.[8] The current study revealed a significant change in liver enzymes during COVID-19 exposure. The reason behind the significant elevation is due to the liver injury caused by the viral infection. Several studies revealed a strong association between liver enzyme elevation and severity of COVID-19, and clearly affecting overall prognosis and mortality rate.[9] However, still the relationship between COVID-19 and liver function is not fully understood.

Current evidence supports that COVID-19-associated liver injury is a multifactorial attack. Several factors may affect liver function along with viral infection. Hypertension, diabetes, coronary heart diseases, kidney dysfunction and malignancy. Different treatments such antiviral, antibiotics, and corticosteroids could have negative impact on liver function.

There have been several studies that have shown an association between COVID-19 and abnormal liver enzyme activities. These studies have found that a significant proportion of COVID-19 patients have elevated levels of liver enzymes, such as ALT and AST, which can indicate

liver injury Table 4. One study published in the Journal of Hepatology in 2020, found that more than 50% of COVID-19 patients had abnormal liver enzyme activities, with elevated levels of ALT and AST being the most common abnormalities. The study also found that these abnormal liver enzyme activities were associated with a more severe illness, and were more common in patients with comorbidities such as obesity and diabetes.[10] Another study published in the Journal of Clinical Medicine in 2020, found that 56% of COVID-19 patients had abnormal liver enzyme, with elevation of ALT and AST. The study also found that patients with abnormal liver enzyme activities had a higher risk of ICU admission and death compared to patients with normal liver enzyme activities.[11]

Table 4: COVID-19 Patients with AST and ALT Elevated Serum from Different Studies.

Source	Country	Time Period	Patients Number	Gender		Age Median (IQR)	Elevated Serum Levels	
				M (%)	F (%)		AST (%)	ALT (%)
Zhao *et al.*[14]	China	January-February 2020	**75**	42 (56%)	33 (44%)	47 (34-55)	14 (19%)	15 (20%)
Zhang *et al.*[15]	China	January-February 2020	82	54 (66%)	28 (34%)	72.5 (65–80)	22 (30.6%)	44 (61.1%)
Richardson *et al.*[16]	USA	March -April 2020	5700	3437(60%)	2263 (40%)	63(52-75)	3263 (58.4%)	2176 (39.0%)
This study	Saudi Arabia	January-June 2021	77	45 (58 %)	33(42%)	58 (12-81)	26 (34%)	9 (12%)

It is not yet fully understood the exact cause of liver injury in COVID-19 patients, it is hypothesized that it may be related to the high levels of inflammation seen in COVID-19 patients, which can cause damage to the liver. It is also thought that the virus may directly infect the liver cells. There are a variety of reasons why patients with COVID-19 have elevated liver enzymes, including underlying liver disease, liver damage caused by drugs, and underlying viral infection. ACE2, the receptor for SARS-CoV-2, can also be found in the liver.[12] Different treatments such antiviral, antibiotics, and corticosteroids could also have negative impact on liver function.[13]

Conclusion

It is important to note that not all cases of abnormal liver enzyme activities in COVID-19 patients lead to serious or long-term liver damage, and the majority of patients with mild to moderate liver enzyme elevation recover completely. However, it is important to monitor liver function in COVID-19 patients, especially those with underlying liver disease or other comorbidities.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical Consideration

All procedures performed in the present study were in accordance with the ethical standards of the Institutional Review Board (IRB) at King Abdullah International Medical Research Center (KAIMRC) in Riyadh, Saudi Arabia at which the study was conducted (Protocol Approval Number SP 21R/200/05).

Informed Consent

Since the current study is a retrospective the consent requirement was waived.

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Author Contributions

R.A conceptualized the idea, and wrote the manuscript. H.A & M.A contributed to the manuscript writing. W.P analyzed data and writing the results. N.A & M. E revised the manuscript. H.A, A.A, M.J, & N.A collected data. All authors reviewed and approved the final draft of the manuscript.

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