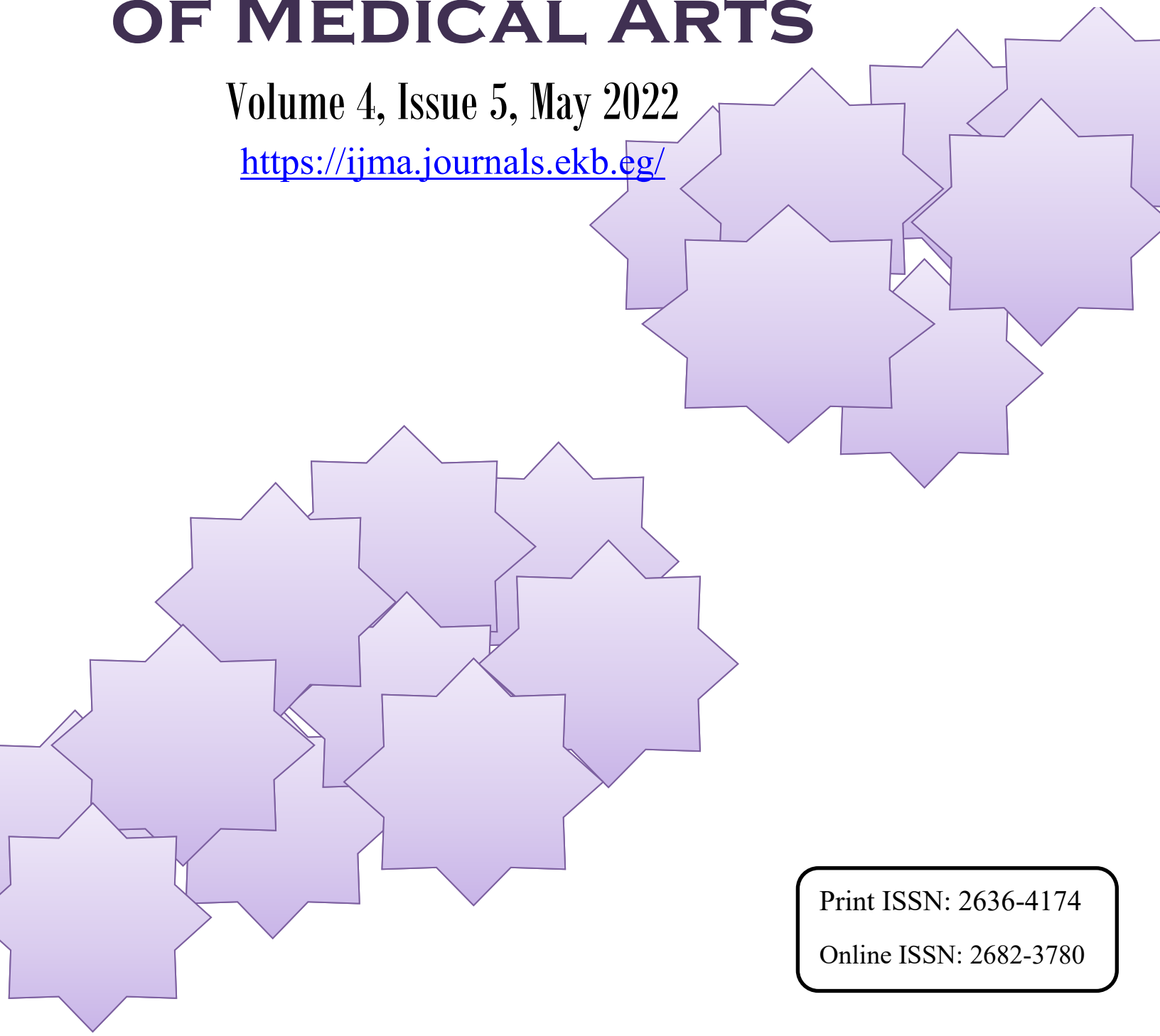
International Journal of Medical Arts

Volume 4, Issue 5, May 2022

https://ijma.journals.ekb.eg/



Print ISSN: 2636-4174

Online ISSN: 2682-3780

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main Subject [Internal Medicine]

Original Article

Evaluation of Some Biochemical and Hematological Parameters in COVID-19 Patients and its Relation to Severity

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Article information

Received: 21-04-2022

Accepted: 26-06-2022

DOI: 10.21608/IJMA.2022.130259.1450

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Citation: Emran TM, Saad AA, Alrifai AW, Al-Hendawy HH. Evaluation of Some Biochemical and Hematological Parameters in COVID-19 Patients and its Relation to Severity. IJMA 2022 May; 4 [5]: 2394-2399. doi: 10.21608/IJMA.2022.130259.1450

ABSTRACT

Background: By the end of 2019, coronavirus identified as a cause of pneumonia cases in Wuhan city, China. In February 2020, World Health Organization reported the disease COVID-19, which means for coronavirus disease 2019. There is a great need for rapid and accurate diagnostic tools to aid in triage of severe cases.

The aim of the work: Our study aimed to evaluate some biochemical and hematological parameters in COVID-19 patients and its relation to severity.

Patients and Methods: It was a case control study, included 200 individuals which had classified into two groups. COVID group: 100 patients with Positive PCR COVID-19 infection. Control group: 100 individuals matched for age and sex and complained of diseases apart from COVID-19 confirmed by negative PCR. All patients were chosen from outpatient clinic and inpatient of Chest department of Al-Azhar University Hospital at New Damietta from March 2021 to January 2022. Evaluation of complete blood picture with differential count, inflammatory profile as CRP, ferritin and LDH together with serum protein electrophoresis were done.

Results: We found that there was markedly difference between COVID-19 group and control group as regards to WBCs, Lymphocyte and PNL/ Lymph ratio. It also found that in COVID-19 group D-Dimer, serum ferritin and LDH were highly significant increase in COVID-19 group compared to control group. Finally, serum protein electrophoresis shows significant changes in COVID-19 group compared to control groups and also shows significant correlation with severity of cases.

Conclusion: We concluded that laboratory tests may serve as adjuvant in diagnosis and following up of COVID-19 cases and using of serum protein electrophoresis may aid in early diagnosis and correlate with severity.

Keywords: COVID-19, D-Dimer, protein electrophoresis, markers of severity.

INTRODUCTION

Coronaviruses are a great family of dangerous pathogens which cause human and animal diseases. By the end of 2019, a pneumonia epidemic in in Wuhan city, China caused by coronavirus brought attention to coronaviruses [1]. It rapidly propagates, result in an epidemic in China, followed by growing number of cases in all the world [2].

In February 2020, World Health Organization reported the disease COVID-19, which means for coronavirus disease 2019 [3]. The virus which causes COVID-19 is dominated severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]; at the past, it was referred to as 2019-nCoV [4].

The guidelines of Chinese health authorities branded three transmission routes for COVID-19 which droplet, contact, and aerosol transmission [5].

Complete clinical symptoms are not defined yet and the reported manifestations range from mild cases to severe cases which even ended by death [6].

The most prevalent reported manifestations are cough, fever, fatigue or myalgia, pneumonia, which complicated by dyspnea, whereas less prevalent reported manifestations include diarrhea, headache, hemoptysis, and phlegm-producing cough and runny nose [7].

Mild cases were cured after 7 days while severe cases were complicated with respiratory failure owing to alveolar damage that may result in death [5].

On February 14, 2020, identification of the first case of COVID-19 was announced in Egypt. Then after, the number of confirmed cases continued to increase to about 500,000 by June 22, 2022 [8].

Early and proper diagnosis and isolation of any suspected patients play an important role in controlling COVID-19 outbreak [9].

THE AIM OF THE WORK

There is a great need to diagnostic markers that can aid the triage of patients most likely to develop a severe form of this outbreak and thereby offer a more adapted clinical management and assist in saving of patients with severe COVID-19 disease.

Our study aimed to evaluate some biochemical and hematological parameters in COVID-19 patients and its relation to severity.

PATIENTS AND METHODS

This observational case control study was conducted at Chest and Clinical Pathology departments of Al-Azhar University Hospital at New Damietta, Egypt during the period from March 2021 to January 2022.

The study included 200 patients and control subjects which had classified into two groups. COVID group included 100 patients complaining of symptoms suggestive of COVID infection admitted to Al-Azhar University Hospital with positive PCR COVID-19 infection at the time of admission with positive signs of CT chest. Control group which included 100 individuals matched for age and sex and complained of diseases apart from COVID-19 confirmed by negative PCR.

All patients were recruited from outpatient clinic and inpatient of Chest department of Al-Azhar University Hospital at New Damietta, Egypt during the period from March 2021 to January 2022. An Informed consent was taken and signed from all patients and controls in compliance with Helsinki Declaration 1975.

Patients with age below 18 years and those with other infectious diseases were excluded from the study.

All included subjects submitted to full history taking, general and local examination, radiological investigations[CT and detection of CORADS categories for severity of pulmonary involvement in COVID cases [10] by pulmonologist] and laboratory investigations at the time of admission including complete blood count with differential count [Sysmex XS-500i Automated Hematology Analyzer, Japan], liver and kidney function tests, high Sensitive C - reactive protein [HR-CRP], Lactate dehydrogenase [LDH], serum ferritin, [Roche Cobas C311 Automated Chemistry Analyzer, Germany]. Also, PCR for confirmation of COVID-19 infection.

Serum protein electrophoresis done by [Capillary Electrophoresis, Minicap Sebia Flex Piercing, French].

Statistical analysis

Using SPSS 22.0 all data were analyzed statistically. Qualitative and categorical data were expressed as numbers and percentages and compared using the Chi-square test or Fisher's exact test, when appropriate. Continuous data were expressed as means ± standard deviations [SD]. For

comparing means between two groups we used the student's t test. Correlation test investigated the relation between CORADS which assess severity of cases and each variable in COVID group. ROC analyses were done for bands of protein electrophoresis to assess diagnostic performance of each band. All statistical tests were two-sided. P values less than 0.05 were considered significant.

RESULTS

The main Results of our study as follow

Age in COVID-19 group was ranged from 19 to 72 years with mean of 45.7 years. 57% of patients were male, 43% ware females, 63% had DM as co-morbidity, 38% were hypertensive and 31% had history of chest diseases. Control group individuals matched for age and sex, 49% had DM as co-morbidity, 33% were hypertensive and 25%,22% had history of chest and cardiac disease respectively. There was no statistically significant difference between both groups in demographic data. Clinical data are summarized in [table 1].

In our study the most frequent radiological findings were Ground glass opacities [49%], Subpleural Consolidation [27%] and Trans lobar consolidation [20%]. While as regards to CO-RADS, there were 6 % had score I, 10% had score II, 30% had score III, 34% had score IV and 20% had score V. [table 2].

As regard to laboratory data, comparisons between COVID-19 group and control group are presented in [table 3].

As regard severity of cases, correlation between CORADS and different parameters in COVID-19 group is presented in [table 4].

Receiver operating characteristic [ROC] analysis was performed to determine value of bands of protein electrophoresis in prediction of severity of COVID-19 infection [figure 1]. Bands of protein electrophoresis especially alpha 1, alpha 2, beta 1 and gamma had good performance in predicting severe COVID-19; hence, the AUC was 0.848 with high statistically significant difference between compared groups.

Table [1]: Clinical Data of COVID group [No. 100]

Symptoms	No[%]
Fever	68
Sore throat	35
Cough	67
Dyspnea	68
Anosmia	18
Diarrhea	22
Vomiting	25
Severity by CORADS	
Mild	16
Moderate	40
Severe	44

Table [2]: Comparison of hematological data between 2 studied groups

	COVID-19 Group		Control Group		P value
	Mean[SD]	SD	Mean	SD	
Hemoglobin [g/dL]	13.3	1.7	12.9	1.6	0.1
WBC [x10^3/ul]	12.9	5.3	9.9	3.5	**0.01***
Neutrophils [x10^3/ul]	10.9	5.3	4.6	4.2	**0.01***
Platelets [x10^3/ul]	383.9	139.7	352	112.9	0.07
Lymphocytes [x10^3/ul]	1.7	0.87	2.47	0.48	**0.001***

Table [3]: Comparison of biochemical data between 2 studied groups

	COVID-19 Group		Control Group		P value
	Mean	**SD**	**Mean**	**SD**	
D-Dimer [mg/ml]	1570.6	867.91	362.9	148	**0.01***
ALT [U/L]	50.8	24.1	36.4	14.1	**0.01***
AST [U/L]	50.2	18.6	39.4	10.8	**0.01***
LDH [U/L]	1491.9	648.6	280.7	81.8	**0.001***
S. Ferritin [ug/L]	890.3	299.2	171.83	22.2	**0.01***
CRP [mg/L]	90.2	25.92	1.73	0.6	**0.01***
Total protein [g/dl]	6.8	0.81	6.2	0.77	**0.002***
Protein electrophoresis					
Albumin [g/dl]	3.6	0.78	4.3	0.6	0.2
Alpha 1 [g/dl]	0.4	0.1	0.2	0.1	0.01*
Alpha 2 [g/dl]	0.8	0.2	0.6	0.2	0.001*
Beta 1 [g/dl]	0.3	0.1	0.4	0.1	0.01*
Beta 2 [g/dl]	0.5	0.2	0.3	0.1	0.90
Gamma [g/dl]	1.2	0.7	0.8	0.2	0.01*

Table [4]: Correlation between CO-RADS [severity] and different parameters in COVID-19 patients

	CORADS	
	r	**p- value**
Age	-0.104	0.524
So2	-0.043	0.793
Hemoglobin	-0.178	0.272
Platelets	0.052	0.751
WBC	-0.248	0.123
Lymphocytes	-0.048	0.770
Neutrophils	-0.134	0.408
D- dimer	.465	**.041***
Urea	0.001	0.993
Creatinine	0.179	0.270
ALT	.190	.084
AST	.197	.072
LDH	.010	**.093**
S. Ferritin	0.157	**.015***
CRP	0.532	**.032***
Alpha 1	0.37	**0.001***
Alpha 2	0.25	**0.001***
Beta 2	0.07	**0.9**
Gamma	0.24	**0.001***

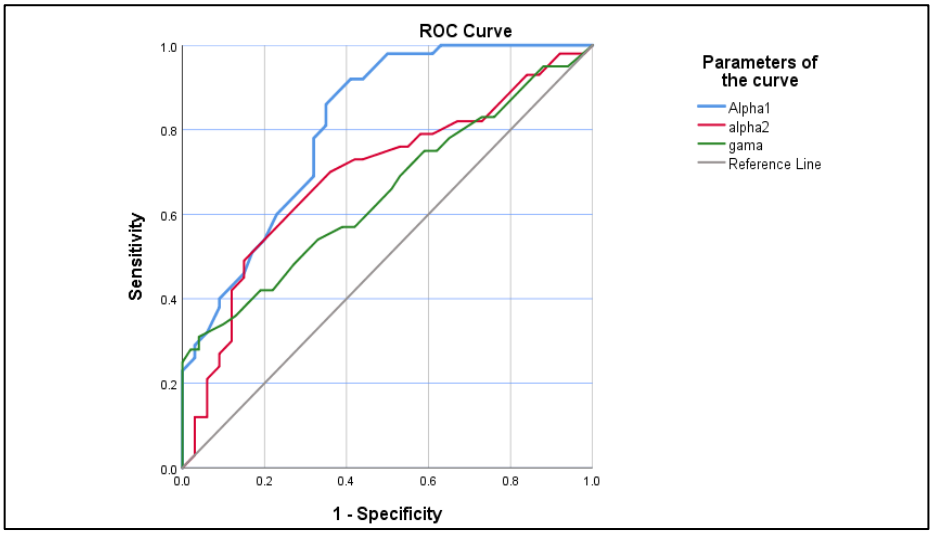

Figure [1]: ROC curve of bands of serum protein electrophoresis in prediction of severity of COVID infection

DISCUSSION

By the end of 2019, coronavirus identified as a cause of pneumonia cases in Wuhan city, China. In February 2020, World Health Organization [WHO] declared COVID-19 as a public health emergency [11]. Early diagnosis of infected patient is helpful and can control infection and spread of this outbreak. There is increasing demand to diagnostic laboratory markers that can help the triage of patients most likely to develop a severe form of COVID 19 and thereby help in clinical management.

Our study aimed to evaluate some biochemical and hematological parameters in COVID-19 patients and its relation to severity as diagnostic prognostic tools

Our study shows highly significant difference between COVID-19 group and healthy group regarding to WBCs, Lymphocyte and PNL/ Lymph Ratio [p <0.001]. Lymphocytes obtained results exhibited that there is a highly significant decrease for patients' group [1.7 × 109/l ± 0.87] compared with healthy group [2.4 × 109/l ± 2.4] with p-value < 0.001. Our results were supported by Yuan *et al.* [12] who found that Lymphocytes results exhibited that there is a highly significant decrease for patients' group [1.7 $\times 10^9$/l ± 0.87] compared with control normal group [2.4 $\times 10^9$/l ± 2.4] with p-value < 0.001. Where lymphopenia is considered the most common hematological parameter in COVID-19 infection. Neutrophil to Lymphocyte ratio [NLR] was also determined for both patients and controls with highly significant difference between 2 studied groups [$p < 0.001$].

As regard biochemical data, our results showed that there was highly statistically significant difference between studied groups in levels of D-Dimer, ALT, AST and LDH between COVID-19 group and healthy group. Also, levels of inflammatory markers as ferritin and H.S CRP showed highly significant difference between COVID-19 group and healthy group.

Our results were in accordance with Khalid *et al.* [13] found that the values of CRP, Ferritin, D-Dimer, AST, ALT showed significant differences between COVID-19 patients and control groups.

In Wuhan, China, in a retrospective study conducted on patients with COVID-19 showed a higher serum ferritin [p < 0.008], raised LDH [$p < 0.001$], than healthy individuals. Higher CRP and ferritin may be associated with ARDS [14].

Elevated CRP levels are in response to infection. In general, the level of CRP in bacterial infection is higher than in viral infection. But, in COVID-19 patients the results revealed a high level of CRP, which are consistent with other studies. Also, higher CRP levels could be a marker to predict the possibility of aggravation of COVID-19 patients, which may help to discover those patients at an early stage for proper treatment. Its concentration is not affected by sex and age. CRP can activate complement inducing phagocytosis. The concentration of CRP is positively correlated to the severity of COVID-19 on computerized tomography [CT] performance; CRP test may be an early biomarker for severe disease and could help clinicians to stratify the patients for ICU [15].

As regard results of protein electrophoresis, which is fully automated instrument and easily operated, showed highly statistically significant difference in levels of alpha 1, alpha 2, beta 1 and gamma bands while in albumin and beta 2 levels showed no statistically significant difference in both studied groups. The changes in bands of electrophoresis are correlated to severity of COVID-19. These finding in results of protein electrophoresis are novel for this study and may be used as diagnostic marker for severity of COVID-19 which helps in early detection of infection and degree of severity and can aid the triage of severely infected patients and helps in proper management.

Conclusion: In this study we concluded that several blood parameters may be used in early diagnosis of COVID-19 and helps in assessment of severity. Serum protein electrophoresis may be a useful tool for accurate and rapid diagnosis of COVID-19 infection.

Conflict of interest:

No conflict of interest

Acknowledgements:

We would like to express our great gratitude and respect to all the healthcare professionals and others who have dedicated themselves to control outbreak of COVID-19.

Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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5/2022

International Journal of Medical Arts

https://ijma.journals.ekb.eg/
Print ISSN: 2636-4174
Online ISSN: 2682-3780